

04/20/98

UPDATE

Page 1

s [ae][hf][wa]s[atslfhnari][nq][lw][lqmr]p[ga]/sqsp

L1 0 [AE][HF][WA]S[ATSLFHNARI][NQ][LW][LQMR]P[GA]/SQSP

=> s [ae][hf][wa]s[atslfhnari][nq][lw][lqmr]p[ga]/sqsfp

L2 0 [AE][HF][WA]S[ATSLFHNARI][NQ][LW][LQMR]P[GA]/SQSFP



08/480494

M.BORIN



04/20/98

UPDATE

Page 1

FILE 'USPATFULL' ENTERED AT 14:23:57 ON 20 APR 1998
L3 90 S LHRH/CLM

=> d bib, kwic 1-10

L3 ANSWER 1 OF 90 USPATFULL
AN 1998:36379 USPATFULL
TI Pharmaceutical preparation for improving the bioavailability of
drugs which are difficult to absorb and a procedure for obtaining
it
IN Garces, Jose de los Santos, Barcelona, Spain
Munoz, Angel Bonilla, Barcelona, Spain
Anton, Jose Maria Garcia, Barcelona, Spain
PA Lipotec S.A., Barcelona, Spain (non-U.S. corporation)
PI US 5736161 980407
AI US 94-278520 940721 (8)
PRAI ES 93-1637 930721
DT Utility
EXNAM Primary Examiner: Spear, James M.
LREP Wigman, Cohen, Leitner & Myers, PC
CLMN Number of Claims: 32
ECL Exemplary Claim: 1
DRWN 5 Drawing Figure(s); 4 Drawing Page(s)
LN.CNT 704
CLM What is claimed is:
 . . . the group consisting of human growth hormone, porcine growth
hormone, bovine growth hormone, human calcitonin, salmon
calcitonin, carbocalcitonin, insulin or **LHRH**;
acetylcholine; hyaluronic acid; alpha-lipoprotein; IgG;
immunomodulators selected from interferon or interleukins;
cyclosporin-A; Arsenaze III; .sup.1 C radioactive labelers;
.sup.90 Te. . .
 . . . the group consisting of human growth hormone, porcine growth
hormone, bovine growth hormone, human calcitonin, salmon
calcitonin, carbocalcitonin, insulin or **LHRH**;
acetylcholine; hyaluronic acid; alpha-lipoprotein; IgG;
immunomodulators selected from interferon or interleukins;
cyclosporin-A; Arsenaze III; .sup.1 C radioactive labelers;
.sup.90 Te. . .
L3 ANSWER 2 OF 90 USPATFULL
AN 1998:36341 USPATFULL
TI Method for preparing radiolabeled peptides
IN Srinivasan, Ananthachari, 332 Woodmere Dr., St. Charles, MO,
United States 63304
PI US 5736120 980407
AI US 96-660262 960607 (8)

08/480494

M.BORIN

DT Utility
EXNAM Primary Examiner: [REDACTED]ght, John; Assistant Examiner: [REDACTED]nes, Dameron
LREP Guffey, Wendell Ray; McBride, Thomas P.
CLMN Number of Claims: 5
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 397
CLM What is claimed is:
 . . . protein receptors, adrenocorticotrophic hormone, atrial
 natriurtic peptides, bradikinins, chemotactic peptides, dynorphin,
 fibronectin fragments, growth hormone releasing peptides,
 Luteinizing Hormone-Releasing Hormone (LHRH),
 Somatostatin (SMS), and Substance P.

L3 ANSWER 3 OF 90 USPATFULL
AN 1998:33599 USPATFULL
TI Male contraceptive implant
IN Moo-Young, Alfred J., Hastings-on-Hudson, NY, United States
Saleh, Saleh I., Queens, NY, United States
PA The Population Council, Center for Biomedical Research, New York,
NY, United States (U.S. corporation)
PI US 5733565 980331
AI US 96-606063 960223 (8)
DT Utility
EXNAM Primary Examiner: Azpuru, Carlos
LREP Lerner, David, Littenberg, Krumholz & Mentlik
CLMN Number of Claims: 36
ECL Exemplary Claim: 1
DRWN 7 Drawing Figure(s); 5 Drawing Page(s)
LN.CNT 964
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
CLM What is claimed is:
 19. The implantable system of claim 1, wherein said sterilitant is
 LHRH or an LHRH analog.

 20. The implantable system of claim 19, wherein said sterilitant
 is LHRH or an LHRH analog.

L3 ANSWER 4 OF 90 USPATFULL
AN 1998:24934 USPATFULL
TI Drug delivery compositions comprising lysophosphoglycerolipid
IN Illum, Lisbeth, Nottingham, United Kingdom
PA Danbiosyst UK Limited, Nottingham, United Kingdom (non-U.S.
corporation)
PI US 5725871 980310
AI US 94-260611 940615 (8)
RLI Continuation of Ser. No. US 92-834296, filed on 18 Feb 1992, now
abandoned
PRAI GB 89-18879 890818
DT Utility
EXNAM Primary Examiner: Kishore, Gollamudi S.
LREP Arnall Golden & Gregory, LLP
CLMN Number of Claims: 10
ECL Exemplary Claim: 1
DRWN 12 Drawing Figure(s); 12 Drawing Page(s)
LN.CNT 642
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
CLM What is claimed is:
 . . . growth hormones, glucagon, interferons, secretin, bradykinin
 antagonists, growth hormone releasing factor, thyrotropin
 releasing hormone, ACTH analogues, insulin-like growth factors,

enkephalins, **LHRH** and analogues, growth hormone releasing hormone, nifedipin, thymic humoral factor, calcitonin gene related peptide, atrial natriuretic peptide, metoclopramide, ergotamine, dihydroergotamine, . . .

L3 ANSWER 5 OF 90 USPATFULL
AN 1998:7163 USPATFULL
TI Process and intermediates for the synthesis of LHRH antagonists
IN Funk, Kenneth W., Lindenhurst, IL, United States
Lundell, Edwin O., Libertyville, IL, United States
Miller, Robert B., Libertyville, IL, United States
Chang, Jane L., Buffalo Grove, IL, United States
Kishore, Vimal, Mundelein, IL, United States
Napier, James J., Lindenhurst, IL, United States
Staeger, Michael A., Greenfield, WI, United States
PA Abbott Laboratories, Abbott Park, IL, United States (U.S. corporation)
PI US 5710247 980120
AI US 96-618674 960319 (8)
DT Utility
EXNAM Primary Examiner: Tsang, Cecilia J.; Assistant Examiner: Celsa, Bennett
LREP Anand, Mona
CLMN Number of Claims: 18
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 2217
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
CLM What is claimed is:
1. A process for preparing an **LHRH** antagonist having the structure Q-D2Nal.sup.1 -D4ClPHe.sup.2 -D3Pal.sup.3 -Ser.sup.4 -NMeTyr.sup.5 -DLys(Nic).sup.6 -Leu.sup.7 -Lys(iPr).sup.8 -Pro.sup.9 DAla.sup.10 NH.sub.2 wherein Q is selected from . . . coupling the unprotecting compound from step (a) with a second oligopeptide compound having the formula Q-D-2Nal-D-4ClPhe-D-3Pal-OH (III) to produce said **LHRH** antagonist.

L3 ANSWER 6 OF 90 USPATFULL
AN 1998:7162 USPATFULL
TI Process for intermediates for the synthesis of LHRH antagonists
IN Funk, Kenneth W., Lindenhurst, IL, United States
Lundell, Edwin O., Libertyville, IL, United States
Miller, Robert B., Libertyville, IL, United States
Chang, Jane L., Buffalo Grove, IL, United States
Kishore, Vimal, Mundelein, IL, United States
Napier, James J., Lindenhurst, IL, United States
Staeger, Michael A., Greenfield, WI, United States
PA Abbott Laboratories, Abbott Park, IL, United States (U.S. corporation)
PI US 5710246 980120
AI US 96-618547 960319 (8)
DT Utility
EXNAM Primary Examiner: Tsang, Cecilia J.; Assistant Examiner: Celsa, Bennett
LREP Anand, Mona
CLMN Number of Claims: 20
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 2271
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
CLM What is claimed is:

1. A process for preparing an **LHRH** antagonist having the structure Q-D2Na^{sup.1} -D4ClPhe^{sup.2} -D3Pal^{sup.3} -Ser^{sup.4} -NMeTyr^{sup.5} -DLys(Nic)^{sup.6} -Leu^{sup.7} -Lys(iPhe)^{sup.8} -Pro^{sup.9} DAla^{sup.10} NH^{sub.2} wherein Q is selected from . . . or both of R^{sup.1} and R^{sup.2} is an --OH protecting group, deprotecting the compound of formula III to produce the **LHRH** antagonist.

L3 ANSWER 7 OF 90 USPATFULL
AN 97:118014 USPATFULL
TI 6-position modified decapeptide **LHRH** antagonists
IN Haviv, Fortuna, Deerfield, IL, United States
Fitzpatrick, Timothy D., Salem, OR, United States
Swenson, Rolf E., Grayslake, IL, United States
Nichols, Charles J., Greendale, WI, United States
Mort, Nicholas A., Waukegan, IL, United States
Greer, Jonathan, Chicago, IL, United States
PA Abbott Laboratories, Abbott Park, IL, United States (U.S. corporation)
PI US 5698522 971216
WO 9413313 940623
AI US 95-446809 950601 (8)
WO 93-US11628 931130
950601 PCT 371 date
950601 PCT 102(e) date
RLI Continuation of Ser. No. US 92-987921, filed on 4 Dec 1992, now abandoned
DT Utility
EXNAM Primary Examiner: Tsang, Cecilia J.; Assistant Examiner: Gupta, Anish
LREP Anand, Mona
CLMN Number of Claims: 6
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 2497
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
CLM What is claimed is:
5. A pharmaceutical composition for inhibiting the release of **LHRH** comprising a therapeutically effective amount of a compound as defined by claim 1 in combination with a pharmaceutically acceptable carrier.
. . .
6. A method of inhibiting **LHRH** release in a mammal in need of such treatment comprising administering to the host animal a therapeutically effective amount of. . .

L3 ANSWER 8 OF 90 USPATFULL
AN 97:93872 USPATFULL
TI Aerosol drug formulations for use with non CFC propellants
IN Adjei, Akwete L., Wadsworth, IL, United States
Gupta, Pramod K., Gurnee, IL, United States
Lu, Mou-Ying Fu, Lake Bluff, IL, United States
PA Abbott Laboratories, Abbott Park, IL, United States (U.S. corporation)
PI US 5676931 971014
AI US 96-655275 960515 (8)
RLI Continuation of Ser. No. US 93-161115, filed on 2 Dec 1993, now abandoned
DT Utility
EXNAM Primary Examiner: Bawa, Raj
LREP Anand, Mona
CLMN Number of Claims: 22

ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 620

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

CLM What is claimed is:
9. A pharmaceutical composition according to claim 8 wherein the medicament is selected from the group consisting of **LHRH** analogs and 5-lipoxygenase inhibitors.

10. A pharmaceutical composition according to claim 1 wherein the medicament is an **LHRH** analog.

L3 ANSWER 9 OF 90 USPATFULL
AN 97:89035 USPATFULL
TI Ionic molecular conjugates of biodegradable polyesters and bioactive polypeptides
IN Shalaby, Shalaby W., Pendleton, SC, United States
Jackson, Steven A., Holliston, MA, United States
Moreau, Jacques-Pierre, Upton, MA, United States
PA Kinerton Limited, Ireland (non-U.S. corporation)
PI US 5672659 970930
WO 9415587 940721
AI US 95-464735 950629 (8)
WO 94-US148 940105
950629 PCT 371 date
950629 PCT 102(e) date
PRAI IE 93-930005 930106
DT Utility
EXNAM Primary Examiner: Nutter, Nathan M.
LREP Fish & Richardson P.C.; McGowan, William E.
CLMN Number of Claims: 32
ECL Exemplary Claim: 1
DRWN 3 Drawing Figure(s); 3 Drawing Page(s)
LN.CNT 985

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

CLM What is claimed is:
10. The composition of claim 1, wherein said polypeptide is chosen from the group consisting of **LHRH**, somatostatin, bombesin/GRP, calcitonin, bradykinin, galanin, MSH, GRF, amylin, tachykinins, secretin, PTH, CGRP, neuromedins, PTHrP, glucagon, neurotensin, ACTH, GHRP, GLP, VIP, . . .
31. A composition of claim 3, wherein said polypeptide is somatostatin or an **LHRH** analog.

L3 ANSWER 10 OF 90 USPATFULL
AN 97:78416 USPATFULL
TI Products for administering an initial high dose of Cetrorelix and producing a combination package for use when treating diseases
IN Engel, Jurgen, Alzenau, Germany, Federal Republic of
Hilgard, Peter, Frankfurt, Germany, Federal Republic of
Reissmann, Thomas, Frankfurt, Germany, Federal Republic of
PA ASTA Medica Aktiengesellschaft, Dresden, Germany, Federal Republic of (non-U.S. corporation)
PI US 5663145 970902
AI US 94-354838 941208 (8)
PRAI DE 93-4342091 931209
DT Utility
EXNAM Primary Examiner: Russel, Jeffrey E.
LREP Cushman Darby & Cushman IP Group of Pillsbury Madison & Sutro LLP
CLMN Number of Claims: 25
ECL Exemplary Claim: 7

CLM What is claimed is:

1. A kit comprising (a) an initial dose of an **LHRH** antagonist suitable for treatment of hormone-dependent conditions, and (b) at least one maintenance dose of the **LHRH** antagonist, in an amount which is insufficient for treating the hormone-dependent conditions when administered alone.
2. The kit of claim 1, wherein the **LHRH** antagonist of (b) is in a slow-releasing formulation.
3. The kit of claim 1, wherein the **LHRH** antagonist is Cetrorelix.
7. A method of treating a hormone-dependent condition which comprises the steps of (a) administering an initial dose of an **LHRH** antagonist to a person having a hormone-dependent condition, and (b) then administering to that person a maintenance dose of an **LHRH** antagonist in an amount which is insufficient for treating the hormone-dependent conditions when administered alone.
8. The method of claim 7, wherein the maintenance dose of the **LHRH** antagonist is a slow-releasing formulation.
9. The method of claim 7, wherein the **LHRH** antagonist is Cetrorelix.
- A method for decreasing male fertility comprising the steps of (a) administering to a male an initial dose of an **LHRH** antagonist, and (b) then administering to that male a maintenance dose of an **LHRH** antagonist in an amount which is insufficient for decreasing male fertility when administered alone.
22. The method of claim 21, wherein the **LHRH** antagonist is Cetrorelix.

08/480494 APS,STN

=> d his

(FILE 'HOME' ENTERED AT 09:40:37 ON 08 AUG 1997)

FILE 'REGISTRY' ENTERED AT 09:41:07 ON 08 AUG 1997
L1 4 S AFASYNLKPA/SQEP

=> d sqd, bib 1-4

L1 ANSWER 1 OF 4 REGISTRY COPYRIGHT 1997 ACS
RN 186837-47-8 REGISTRY
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL 10
NTE modified

type	location		description
terminal mod.	Ala-1	-	N-acetyl
terminal mod.	Ala-10	-	C-terminal amide
modification	-	-	undetermined modification
modification	Ala-1	-	2-naphthalenyl<2-Naph>
modification	Phe-2	-	chloro<Cl>
modification	Ala-3	-	3-pyridinyl<3Py>
modification	Tyr-5	-	methyl<Me>
modification	Lys-8	-	1-methylethyl<i-Pr>

SEQ 1 AFASYNLKPA
=====

HITS AT: 1-10

AN 126:152828 CA

TI LHRH antagonist synthetic peptide analogs for use as cancer
inhibitors, contraceptives, or other pharmaceuticals

IN Roeske, Roger W.

PA Indiana University Foundation, USA; Roeske, Roger W.

SO PCT Int. Appl., 52 pp.

CODEN: PIXXD2

PI WO 9640757 A2 961219

DS W: AU, CA, JP, US

RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT,
SE

AI WO 96-US9852 960607

PRAI US 95-480494 950607

DT Patent

LA English

REFERENCE 1

AN 126:152828 CA

TI LHRH antagonist synthetic peptide analogs for use as cancer
inhibitors, contraceptives, or other pharmaceuticals

IN Roeske, Roger W.

PA Indiana University Foundation, USA; Roeske, Roger W.

SO PCT Int. Appl., 52 pp.

CODEN: PIXXD2

M. Borin

08/08/97

08/480,494

08/480494 APS,STN

PI WO 9640757 A2 961219
DS W: AU, CA, JP, US
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT,
SE
AI WO 96-US9852 960607
PRAI US 95-480494 950607
DT Patent
LA English

L1 ANSWER 2 OF 4 REGISTRY COPYRIGHT 1997 ACS
RN 186835-69-8 REGISTRY
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL 10
NTE modified

type	location	description
terminal mod.	Ala-1	N-acetyl
terminal mod.	Ala-10	C-terminal amide
modification	-	undetermined modification
modification	Ala-1	2-naphthalenyl<2-Naph>
modification	Phe-2	chloro<Cl>
modification	Ala-3	3-pyridinyl<3Py>
modification	Lys-8	1-methylethyl<i-Pr>

SEQ 1 AFASYNLKPA

=====

HITS AT: 1-10
AN 126:152828 CA
TI LHRH antagonist synthetic peptide analogs for use as cancer
inhibitors, contraceptives, or other pharmaceuticals
IN Roeske, Roger W.
PA Indiana University Foundation, USA; Roeske, Roger W.
SO PCT Int. Appl., 52 pp.
CODEN: PIXXD2
PI WO 9640757 A2 961219
DS W: AU, CA, JP, US
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT,
SE
AI WO 96-US9852 960607
PRAI US 95-480494 950607
DT Patent
LA English

REFERENCE 1

AN 126:152828 CA
TI LHRH antagonist synthetic peptide analogs for use as cancer
inhibitors, contraceptives, or other pharmaceuticals
IN Roeske, Roger W.
PA Indiana University Foundation, USA; Roeske, Roger W.
SO PCT Int. Appl., 52 pp.
CODEN: PIXXD2
PI WO 9640757 A2 961219
DS W: AU, CA, JP, US
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT,
M. Borin 08/08/97

08/480494 APS,STN

SE
AI WO 96-US9852 960607
PRAI US 95-480494 950607
DT Patent
LA English

L1 ANSWER 3 OF 4 REGISTRY COPYRIGHT 1997 ACS
RN 186835-68-7 REGISTRY
FS 3D CONCORD; PROTEIN SEQUENCE; STEREOSEARCH
SQL 10
NTE modified

type	location		description
terminal mod.	Ala-1	-	N-acetyl
terminal mod.	Ala-10	-	C-terminal amide
modification	Ala-1	-	2-naphthalenyl<2-Naph>
modification	Phe-2	-	chloro<Cl>
modification	Ala-3	-	3-pyridinyl<3Py>
modification	Lys-8	-	1-methylethyl<i-Pr>

SEQ 1 AFASYNLKPA

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HITS AT: 1-10

L1 ANSWER 4 OF 4 REGISTRY COPYRIGHT 1997 ACS
RN 183552-38-7 REGISTRY
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL 10
NTE modified

type	location		description
terminal mod.	Ala-1	-	N-acetyl
terminal mod.	Ala-10	-	C-terminal amide
modification	Ala-1	-	2-naphthalenyl<2-Naph>
modification	Phe-2	-	chloro<Cl>
modification	Ala-3	-	3-pyridinyl<3Py>
modification	Tyr-5	-	methyl<Me>
modification	Lys-8	-	1-methylethyl<i-Pr>

SEQ 1 AFASYNLKPA

=====

HITS AT: 1-10

=> d his

(FILE 'HOME' ENTERED AT 09:40:37 ON 08 AUG 1997)

FILE 'REGISTRY' ENTERED AT 09:41:07 ON 08 AUG 1997

L1 4 S AFASYNLKPA/SQEP
L2 1 S 183552-38-7/RN

FILE 'CAPLUS, MARPAT' ENTERED AT 09:51:47 ON 08 AUG 1997

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08/480494 APS,STN

FILE 'CAPLUS, MARPAT' ENTERED AT 09:51:58 ON 08 AUG 1997

FILE 'REGISTRY' ENTERED AT 09:52:22 ON 08 AUG 1997

SET SMARTSELECT ON

L3 SEL L2 1- CHEM : 4 TERMS
SET SMARTSELECT OFF

FILE 'CAPLUS, MARPAT' ENTERED AT 09:52:23 ON 08 AUG 1997

L4 0 FILE CAPLUS

L5 0 FILE MARPAT

TOTAL FOR ALL FILES

L6 0 S L3

FILE 'REGISTRY' ENTERED AT 09:55:10 ON 08 AUG 1997

=> d l1 lc 1-4

L1 ANSWER 1 OF 4 REGISTRY COPYRIGHT 1997 ACS

LC STN Files: CA, CAPLUS, TOXLIT

L1 ANSWER 2 OF 4 REGISTRY COPYRIGHT 1997 ACS

LC STN Files: CA, CAPLUS, TOXLIT

L1 ANSWER 3 OF 4 REGISTRY COPYRIGHT 1997 ACS

L1 ANSWER 4 OF 4 REGISTRY COPYRIGHT 1997 ACS

<-----User Break----->

=> so the first two hits are the same case; entries 3 and 4 do not have related references

'SO' IS NOT A RECOGNIZED COMMAND

COMMAND STACK INTERRUPTED. ENTER "DISPLAY HISTORY"
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=> s afasy.lkpa/sqep

GAPS, WILDCARDS, AND BRACKETS ARE INVALID FOR "EXACT" SEQUENCE FIELD CODES.

=> s afasy.lkpa/sqsp and sql<11

406 AFASY.LKPA/SQSP

183654 SQL<11

L7 406 AFASY.LKPA/SQSP AND SQL<11

=> file caplus,marpat

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

38.84

138.43

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08/08/97

08/480494 APS,STN

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=> s 17<chem>

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COST IN U.S. DOLLARS	SINCE FILE	TOTAL
FULL ESTIMATED COST	ENTRY	SESSION
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DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
CA SUBSCRIBER PRICE	ENTRY	SESSION
	0.00	-0.46

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SET COMMAND COMPLETED

SEL L7 1- CHEM
SELECT IS APPROXIMATELY 89% COMPLETE
L8 SEL L7 1- CHEM : 414 TERMS

SET SMARTSELECT OFF
SET COMMAND COMPLETED

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CA SUBSCRIBER PRICE	ENTRY	SESSION
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08/480494 APS,STN

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S L8
L9 60 FILE CAPLUS
L10 0 FILE MARPAT

TOTAL FOR ALL FILES
L11 60 L8

=> file uspatfull

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	1119.36	1266.77
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
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FILE 'USPATFULL' ENTERED AT 10:03:25 ON 08 AUG 1997
CA INDEXING COPYRIGHT (C) 1997 AMERICAN CHEMICAL SOCIETY (ACS)

FILE COVERS 1971 TO PATENT PUBLICATION DATE: 5 Aug 1997 (19970805/PD)
FILE LAST UPDATED: 6 Aug 1997 (970806/ED)
HIGHEST PATENT NUMBER: US5655220
CA INDEXING IS CURRENT THROUGH 6 Aug 1997 (970806/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 5 Aug 1997 (19970805/PD)
REVISED CLASS FIELDS (/NCL) CURRENT THROUGH: JUN 1997
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: APR 1997

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>>> USPTO/MOC subject headings and subheadings. Thesauri are also <<<
>>> available for the WIPO International Patent Classification <<<
>>> (IPC) Manuals, editions 1-6, in the /IC1, /IC2, /IC3, /IC4, <<<
>>> /IC5, and /IC (/IC6) fields, respectively. The thesauri in <<<
>>> the /IC5 and /IC fields include the corresponding catchword <<<
>>> terms from the IPC subject headings and subheadings. <<<

This file contains CAS Registry Numbers for easy and accurate
substance identification.

=> s 17<chem>

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M. Borin 08/08/97

08/480494 APS,STN

COST IN U.S. DOLLARS	SINCE FILE	TOTAL
FULL ESTIMATED COST	ENTRY	SESSION
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DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
CA SUBSCRIBER PRICE	ENTRY	SESSION
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FILE 'REGISTRY' ENTERED AT 10:03:36 ON 08 AUG 1997
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SET SMARTSELECT ON
SET COMMAND COMPLETED

SEL L7 1- CHEM
L12 SEL L7 1- CHEM : 414 TERMS

SET SMARTSELECT OFF
SET COMMAND COMPLETED

COST IN U.S. DOLLARS	SINCE FILE	TOTAL
FULL ESTIMATED COST	ENTRY	SESSION
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DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
CA SUBSCRIBER PRICE	ENTRY	SESSION
	0.00	-0.46

FILE 'USPATFULL' ENTERED AT 10:03:57 ON 08 AUG 1997
CA INDEXING COPYRIGHT (C) 1997 AMERICAN CHEMICAL SOCIETY (ACS)

S L12
SEARCH OF L12 IS APPROXIMATELY 38% COMPLETE
L13 1 L12

=> d bib,hit

L13 ANSWER 1 OF 1 USPATFULL
AN 96:9277 USPATFULL
TI Compositions and method for the sublingual or buccal
administration therapeutic agents
IN Lu, Mou-Ying F., Lake Bluff, IL, United States
Reiland, Thomas L., Gages Lake, IL, United States
PA Abbott Laboratories, Abbott Park, IL, United States (U.S.
corporation)
PI US 5487898 960130
AI US 94-193374 940207 (8)
DCD 20110208
RLI Continuation-in-part of Ser. No. US 92-983111, filed on 30 Nov
1992, now patented, Pat. No. US 5284657 which is a continuation of
Ser. No. US 91-750843, filed on 26 Aug 1991, now abandoned
M. Borin 08/08/97

08/480494 APS,STN

DT Utility
EXNAM Primary Examiner: Azpuru, Carlos A.
LREP Janssen, Jerry F.
CLMN Number of Claims: 13
ECL Exemplary Claim: 1
DRWN 4 Drawing Figure(s); 4 Drawing Page(s)
LN.CNT 952
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
DETD Particularly preferred LHRH-active peptides and pseudo-peptides for inclusion in formulations of the present invention are the nona- and decapeptides known by the generic names or designations **A-75998**, buserelin, decapeptyl, deslorelin, goserelin, histrelin, nafarelin.
DETD **A-75998** (Sequence I.D. No. 1) is disclosed and claimed in U.S. Pat. No. 5,110,904 and has the structural formula:

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	6.45	1282.59
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	0.00	-0.46

FILE 'CAPLUS' ENTERED AT 10:06:58 ON 08 AUG 1997
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FILE COVERS 1967 - 8 Aug 1997 VOL 127 ISS 6
FILE LAST UPDATED: 8 Aug 1997 (970808/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

Improved currency of Japanese patents. See HELP JCURR.

=> d his

(FILE 'HOME' ENTERED AT 09:40:37 ON 08 AUG 1997)

FILE 'REGISTRY' ENTERED AT 09:41:07 ON 08 AUG 1997

L1 4 S AFASYNLKPA/SQEP
L2 1 S 183552-38-7/RN

FILE 'CAPLUS, MARPAT' ENTERED AT 09:51:47 ON 08 AUG 1997

FILE 'CAPLUS, MARPAT' ENTERED AT 09:51:58 ON 08 AUG 1997
M. Borin 08/08/97

08/480494 APS,STN

FILE 'REGISTRY' ENTERED AT 09:52:22 ON 08 AUG 1997
SET SMARTSELECT ON
L3 SEL L2 1- CHEM : 4 TERMS
SET SMARTSELECT OFF

FILE 'CAPLUS, MARPAT' ENTERED AT 09:52:23 ON 08 AUG 1997
L4 0 FILE CAPLUS
L5 0 FILE MARPAT
TOTAL FOR ALL FILES
L6 0 S L3

FILE 'REGISTRY' ENTERED AT 09:55:10 ON 08 AUG 1997
L7 406 S AFASY.LKPA/SQSP AND SQL<11

FILE 'CAPLUS, MARPAT' ENTERED AT 10:02:02 ON 08 AUG 1997

FILE 'REGISTRY' ENTERED AT 10:02:12 ON 08 AUG 1997
SET SMARTSELECT ON
L8 SEL L7 1- CHEM : 414 TERMS
SET SMARTSELECT OFF

FILE 'CAPLUS, MARPAT' ENTERED AT 10:02:52 ON 08 AUG 1997
L9 60 FILE CAPLUS
L10 0 FILE MARPAT
TOTAL FOR ALL FILES
L11 60 S L8

FILE 'USPATFULL' ENTERED AT 10:03:25 ON 08 AUG 1997

FILE 'REGISTRY' ENTERED AT 10:03:36 ON 08 AUG 1997
SET SMARTSELECT ON
L12 SEL L7 1- CHEM : 414 TERMS
SET SMARTSELECT OFF

FILE 'USPATFULL' ENTERED AT 10:03:57 ON 08 AUG 1997
L13 1 S L12

FILE 'CAPLUS' ENTERED AT 10:06:58 ON 08 AUG 1997

=> s l11 and (LHRH or GnRH or luteinizing or gonadotropin)

8537 LHRH
2 LHRHS
8537 LHRH
(LHRH OR LHRHS)
5228 GNRH
62 GNRHS
5230 GNRH
(GNRH OR GNRHS)
10201 LUTEINIZING
30695 GONADOTROPIN
12217 GONADOTROPINS
32933 GONADOTROPIN
(GONADOTROPIN OR GONADOTROPINS)
L14 59 L9 AND (LHRH OR GNRH OR LUTEINIZING OR GONADOTROPIN)

M. Borin 08/08/97

=> d his

(FILE 'HOME' ENTERED AT 09:40:37 ON 08 AUG 1997)

L1 FILE 'REGISTRY' ENTERED AT 09:41:07 ON 08 AUG 1997
 L2 4 S AFASYNLKPA/SQEP
 1 S 183552-38-7/RN

FILE 'CAPLUS, MARPAT' ENTERED AT 09:51:47 ON 08 AUG 1997

FILE 'CAPLUS, MARPAT' ENTERED AT 09:51:58 ON 08 AUG 1997

L3 FILE 'REGISTRY' ENTERED AT 09:52:22 ON 08 AUG 1997
 SET SMARTSELECT ON
 SEL L2 1- CHEM : 4 TERMS
 SET SMARTSELECT OFF

L4 FILE 'CAPLUS, MARPAT' ENTERED AT 09:52:23 ON 08 AUG 1997
 0 FILE CAPLUS
 L5 0 FILE MARPAT
 TOTAL FOR ALL FILES
 L6 0 S L3

L7 FILE 'REGISTRY' ENTERED AT 09:55:10 ON 08 AUG 1997
 406 S AFASY.LKPA/SQSP AND SQL<11

FILE 'CAPLUS, MARPAT' ENTERED AT 10:02:02 ON 08 AUG 1997

L8 FILE 'REGISTRY' ENTERED AT 10:02:12 ON 08 AUG 1997
 SET SMARTSELECT ON
 SEL L7 1- CHEM : 414 TERMS
 SET SMARTSELECT OFF

L9 FILE 'CAPLUS, MARPAT' ENTERED AT 10:02:52 ON 08 AUG 1997
 60 FILE CAPLUS
 L10 0 FILE MARPAT
 TOTAL FOR ALL FILES
 L11 60 S L8

FILE 'USPATFULL' ENTERED AT 10:03:25 ON 08 AUG 1997

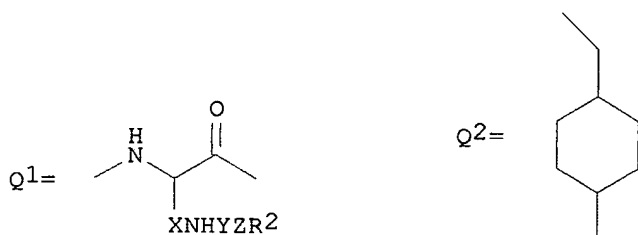
L12 FILE 'REGISTRY' ENTERED AT 10:03:36 ON 08 AUG 1997
 SET SMARTSELECT ON
 SEL L7 1- CHEM : 414 TERMS
 SET SMARTSELECT OFF

L13 FILE 'USPATFULL' ENTERED AT 10:03:57 ON 08 AUG 1997
 1 S L12

L14 FILE 'CAPLUS' ENTERED AT 10:06:58 ON 08 AUG 1997
 59 S L11 AND (LHRH OR GNRH OR LUTEINIZING OR GONADOTROPIN)

=> d an,au,ti,so,abs,kwic 24,25,29,30,45,50,58

AN 1995:573685 CAPLUS
 DN 123:33649
 IN Greer, Jonathan; Haviv, Fortuna; Fitzpatrick, Timothy D.; Swenson, Rolf E.; Nichols, Charles J.; Mort, Nicholas A.
 TI Preparation of 6-position modified decapeptide **LHRH** antagonists
 SO PCT Int. Appl., 86 pp.
 CODEN: PIXXD2
 GI



AB A-D-E-G-J-L-M-Q-R-T [A = N-acetyl-D-3-(naphth-2-yl)alanyl, N-acetyl-D-phenylalanyl, N-acetylsarcosyl, etc.; D = D-Phe, D-3-(4-chlorophenyl)alanyl, D-3-(4-fluorophenyl)alanyl, etc.; E = D-3-(pyrid-3-yl)alanyl, D-3-(thiazol-2-yl)alanyl, etc.; G = Ser, Ser(OBzl), etc.; J = N(R1)-L-[3-(4-(3-amino-1,2,4-triazol-5-yl)aminophenyl)]alanyl, N(R1)-L-tyrosyl, N(R1)-L-homoarginyl, etc.; R1 = H, alkyl; L = Q1; X = (CH2)n, Q2; n = 1-6; Y = D- or L-Ala, 4-aminobutyl, 5-aminopentanoyl, azaglycyl, D-leucyl, D-valyl, etc.; Z = null, D-alanyl, azaglycyl, Gly, D-cyclohexylalanyl, D-His, D-Phe, etc.; R2 = 3-amino-1,2,4-triazol-5-yl, Ac, biotinyl, 2-furoyl, isonicotinoyl, (substituted) PhCO, etc.; M = Leu, Val, L-cyclohexylalanyl, etc. Q = L-citrullyl, L-homocitrullyl, Arg, etc.; R = Pro, N(R1)-Ala; T = NHET, D-alanylamine, D-serylamine, sarcosamide, etc.], were prep'd. Thus, Ac-D-2-Nal-D-4-Cl-Phe-D-3-Pal-Ser-NMeTyr-D-Lys(N.epsilon.-glycylnicotinoyl)-Leu-Lys(N.epsilon.-isopropyl)-Pro-D-Ala-NH2 [2-Nal = 3-(naphth-2-yl)alanyl, 4-Cl-Phe = 3-(4-chlorophenyl)alanyl, 3-Pal = 3-(pyrid-3-yl)alanyl], prep'd. on methylbenzhydrylamine resin, antagonized **LHRH** with pA2 = 11.45.

TI Preparation of 6-position modified decapeptide **LHRH** antagonists

AB . . . etc.], were prep'd. Thus, Ac-D-2-Nal-D-4-Cl-Phe-D-3-Pal-Ser-NMeTyr-D-Lys(N.epsilon.-glycylnicotinoyl)-Leu-Lys(N.epsilon.-isopropyl)-Pro-D-Ala-NH2 [2-Nal = 3-(naphth-2-yl)alanyl, 4-Cl-Phe = 3-(4-chlorophenyl)alanyl, 3-Pal = 3-(pyrid-3-yl)alanyl], prep'd. on methylbenzhydrylamine resin, antagonized **LHRH** with pA2 = 11.45.

ST decapeptide prepn **lhrh** antagonist; peptide deca prepn **lhrh** antagonist

IT Peptides, preparation

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of 6-position modified decapeptide **LHRH**)

M. Borin 08/08/97

antagonists)

IT **163333-60-6P**

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of 6-position modified decapeptide 294LHRH antagonists)

IT 163333-59-3P 163333-61-7P 163333-62-8P **163333-63-9P**
163333-64-0P 163333-65-1P 163333-66-2P
 163333-67-3P 163333-68-4P 163333-69-5P 163333-70-8P
 163333-71-9P 163333-72-0P 163333-73-1P 163333-74-2P
 163333-75-3P 163333-76-4P 163333-77-5P 163333-78-6P
 163333-79-7P **163333-80-0P 163333-81-1P**
163333-82-2P 163333-83-3P 163333-84-4P
163333-85-5P 163333-86-6P 163333-87-7P
163333-88-8P 163333-89-9P 163333-90-2P
163333-91-3P 163333-92-4P 163333-93-5P
163333-94-6P 163333-95-7P 163333-96-8P
163333-97-9P 163333-98-0P 163333-99-1P
163334-00-7P 163334-01-8P 163334-02-9P
163334-03-0P 163334-04-1P 163334-05-2P
163334-06-3P 163334-07-4P 163334-08-5P
163334-09-6P 163334-10-9P 163334-11-0P
163334-12-1P 163334-13-2P 163334-14-3P
163334-15-4P 163334-16-5P 163334-17-6P
 163334-18-7P 163334-19-8P 163334-20-1P 163334-21-2P
 163334-22-3P 163334-23-4P 163334-24-5P 163334-25-6P
 163334-26-7P **163334-27-8P 163334-28-9P**
163334-29-0P 163334-30-3P 163334-31-4P
 163334-32-5P **163334-33-6P 163334-34-7P**
163334-35-8P 163334-36-9P 163334-37-0P
 163334-38-1P 163334-39-2P 163334-40-5P 163334-41-6P
 163334-42-7P 163334-43-8P 163334-44-9P 163334-45-0P
 163334-46-1P 163334-47-2P **163334-48-3P**
163334-49-4P 163334-50-7P 163334-51-8P
163334-52-9P 163334-53-0P 163334-54-1P
163334-55-2P 163334-56-3P 163334-57-4P
 163334-58-5P 163334-59-6P 163334-60-9P 163334-61-0P
 163334-62-1P 163334-63-2P 163334-64-3P 163334-65-4P
 163334-66-5P 163334-67-6P 163334-68-7P 163334-69-8P
 163334-70-1P 163334-71-2P 163334-72-3P 163334-73-4P
 163334-74-5P 163334-75-6P 163334-76-7P 163334-77-8P
 163334-78-9P 163334-79-0P 163334-80-3P 163334-81-4P
 163334-82-5P 163334-83-6P 163334-84-7P 163334-85-8P
 163334-86-9P 163334-87-0P 163334-88-1P 163334-89-2P
 163334-90-5P 163334-91-6P 163334-92-7P **163334-93-8P**
 163334-94-9P **163334-95-0P 163334-96-1P**
 163334-97-2P 163334-98-3P 163334-99-4P 163335-00-0P
 163335-01-1P 163335-02-2P 163335-03-3P 163335-04-4P
 163335-05-5P 163335-06-6P 163335-07-7P 163335-08-8P
 163335-09-9P 163335-10-2P 163335-11-3P 163335-12-4P
 163335-13-5P 163335-14-6P 163335-15-7P 163335-16-8P
 163335-17-9P 163335-18-0P **163335-19-1P**
163335-20-4P 163335-21-5P 163335-22-6P
163335-23-7P 163335-24-8P 163335-25-9P
163335-26-0P 163335-27-1P 163335-28-2P
163335-29-3P 163335-30-6P 163335-31-7P
163335-32-8P 163335-33-9P 163335-34-0P 163335-35-1P

163335-36-2P 163335-37-3P 163335-38-4P 163335-39-5P
 163335-42-0P **163335-43-1P 163335-44-2P**
 163335-45-3P **163335-46-4P 163335-47-5P**
163335-48-6P 163335-50-0P 163335-51-1P
163335-53-3P 163335-54-4P 163335-55-5P 163335-57-7P
 163335-59-9P 163335-60-2P 163335-62-4P 163335-63-5P
 163335-65-7P 163335-66-8P **163335-67-9P**
163335-68-0P 163335-69-1P 163335-70-4P
 163335-71-5P **163335-72-6P 163335-73-7P**
163335-74-8P 163335-75-9P 163335-76-0P 163335-77-1P
 163335-78-2P 163335-79-3P 163335-80-6P 163335-81-7P
 163335-82-8P 163335-83-9P **163335-84-0P**
163335-86-2P 163335-88-4P 163335-90-8P
163335-92-0P 163335-94-2P 163335-96-4P 163335-98-6P
163335-99-7P 163336-01-4P 163336-03-6P
163336-04-7P 163336-05-8P 163336-07-0P
 163336-09-2P 163336-11-6P 163336-13-8P 163336-20-7P
 163437-60-3P

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of 6-position modified decapeptide **LHRH** antagonists)

IT 163437-61-4P 163437-62-5P 163437-63-6P 163437-64-7P
 163437-66-9P 163437-67-0P 163437-68-1P 163437-69-2P
 163437-70-5P 163437-71-6P 163437-72-7P 163437-73-8P
 163437-74-9P 163437-75-0P 163437-76-1P 163437-77-2P
 163437-78-3P 163437-79-4P 163437-80-7P 163437-81-8P
 163437-82-9P 163437-83-0P 163437-84-1P 163437-85-2P
 163437-86-3P 163437-87-4P 163512-26-3P

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of 6-position modified decapeptide **LHRH** antagonists)

IT 9034-40-6, **Lhrh**

RL: BPR (Biological process); BIOL (Biological study); PROC (Process)

(prepn. of 6-position modified decapeptide **LHRH** antagonists)

IT 88-14-2, 2-Furoic acid 107-15-3, 1,2-Ethanediamine, reactions
 109-76-2, 1,3-Propanediamine 110-85-0, Piperazine, reactions
 138-59-0, Shikimic acid 553-53-7, Nicotinic acid hydrazide
 3303-84-2, BOC-.beta.-Ala-OH 3326-71-4, 2-Furoic acid hydrazide
 5818-15-5 13139-15-6, BOC-Leu-OH 13734-36-6D, BOC-Sar-OH, resin
 bound 13836-37-8, BOC-Arg(Tos)-OH 15761-39-4, BOC-Pro-OH
 23680-31-1 27219-07-4 29022-11-5, FMOC-Gly-OH 60142-89-4
 76985-10-9 98266-33-2 115186-31-7 125323-99-1 163335-40-8
 163336-14-9 163336-15-0 163336-18-3

RL: RCT (Reactant)

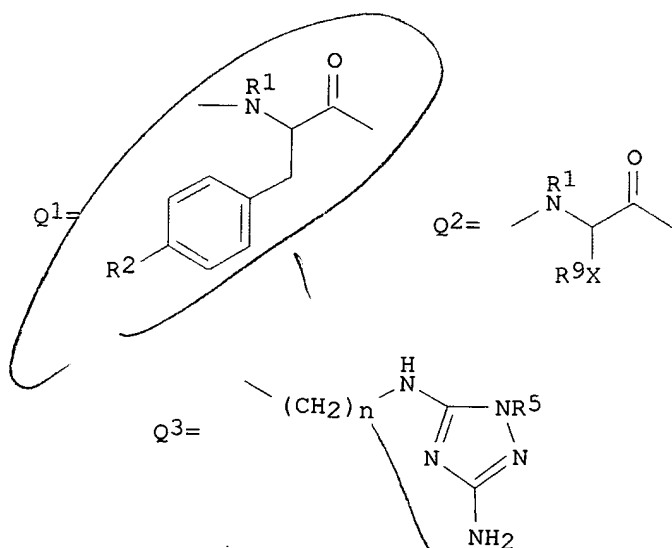
(prepn. of 6-position modified decapeptide **LHRH** antagonists)

IT 163336-16-1DP, resin bound 163336-17-2DP, resin bound

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)

(prepn. of 6-position modified decapeptide **LHRH** antagonists)

L14 ANSWER 25 OF 59 CAPLUS COPYRIGHT 1997 ACS
 AN 1995:397087 CAPLUS
 DN 122:161380
 IN Haviv, Fortuna; Greer, Jonathan; Swenson, Rolf E.; Sauer, Daryl R.
 TI Preparation of **LHRH** antagonists having modified aminoacid
 residues at postions 5 and 6.
 SO PCT Int. Appl., 60 pp.
 CODEN: PIXXD2
 GI



AB A1B2C3D4E5F6G7H8I9J10 [A1 = N-acetyl-D-3-(2-naphthyl)alanyl, Ac-Sar, N-acetylazaglycyl, Ac-D-Phe, etc.; B1 = D-Phe, D-3-(4-chlorophenyl)alanyl, D-3-(2-naphthyl)alanyl, etc.; C3 = D-3-(3-pyridyl)alanyl, D-3-(2-thiazolyl)alanyl, etc.; D4 = Ser, N(R1)-substituted Ser; R1 = alkyl; E5 = Q1, Q2; R2 = NO2, CH2Cl, CH2OH, CH2N3, CH2CN, (CH2)_mNR3R4, Q3, etc.; R3, R4 = H, alkyl, (substituted) Ph, PhCH2; NR3R4 = pyrrolidinyl, piperidinyl, morpholinyl, etc.; R5 = H, alkyl; m = 1,2; n = 0-2; X = 1,4-cyclohexylene, alkylene; R9 = (CH2)_mNR3R4, Q3, etc.; F6 = D-Trp, D-3-(3-pyridyl)alanyl, D-Ser, Q1, etc.; G7 = Leu, N(R1)-substituted Leu, Val, cyclohexylalanyl, Ile, etc.; H8 = (.epsilon.-N-isopropyl)lysyl, N(R1)-substituted Arg; I9 = Pro, N(R1)-substituted Ala; J10 = NHet, D-Ala-NH2, Sar-NH2, D-Ser-NH2, etc.; with the proviso that when J = NHet, then I = Pro], were prepd. Thus, Ac-D-2Nal-D-Phe(4-Cl)-D-3Pal-Ser-NMePhe(4-NO2)-D-Cit-Leu-Arg-Pro-D-Ala-NH2, [2Nal = 3-(2-naphthyl)alanyl, 3Pal = 3-(pyrid-2-yl)alanyl, Cit = citrullyl] prepd. using BOC-protected amino acids and methylbenzhydrylamine resin, antagonized **LHRH** with pA2 = 11.26 using the methods of F. Haviv.

TI Preparation of **LHRH** antagonists having modified aminoacid residues at postions 5 and 6.

AB . . . Thus, Ac-D-2Nal-D-Phe(4-Cl)-D-3Pal-Ser-NMePhe(4-NO2)-D-Cit-Leu-Arg-Pro-D-Ala-NH2, [2Nal = 3-(2-naphthyl)alanyl, 3Pal =

3-(pyrid-2-yl)alanyl, Cit = citrullyl] prepd. using BOC-protected amino acids and methylbenzhydrylamine resin, antagonized **LHRH** with pA2 = 11.26 using the methods of F. Haviv.

ST peptide prepn **LHRH** antagonist

IT Peptides, preparation

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of **LHRH** antagonists having modified aminoacid residues at postions 5 and 6)

IT Hormones

RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(sex, suppression; prepn. of **LHRH** antagonists having modified aminoacid residues at postions 5 and 6)

IT 160618-03-1P 161356-78-1P 161356-79-2P **161356-80-5P**
161356-81-6P 161356-82-7P 161356-83-8P 161356-84-9P
161356-85-0P 161356-86-1P 161356-87-2P 161356-88-3P
161356-89-4P 161356-90-7P 161356-91-8P 161356-92-9P
161356-93-0P **161356-94-1P 161356-95-2P**
161356-96-3P 161356-97-4P

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of **LHRH** antagonists having modified aminoacid residues at postions 5 and 6)

IT 9034-40-6, **LHRH**

RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(prepn. of **LHRH** antagonists having modified aminoacid residues at postions 5 and 6)

IT 13139-15-6 13836-37-8 15761-39-4 23680-31-1 35320-22-0D,
H-D-Ala-NH₂, methylbenzhydrylamine resin-bound 57292-44-1
70663-56-8, BOC-NMePhe(4-NO₂)-OH 76985-10-9 98266-33-2
121080-95-3, BOC-D-Cit 160618-04-2

RL: RCT (Reactant)
(prepn. of **LHRH** antagonists having modified aminoacid residues at postions 5 and 6)

L14 ANSWER 29 OF 59 CAPLUS COPYRIGHT 1997 ACS

AN 1995:183925 CAPLUS

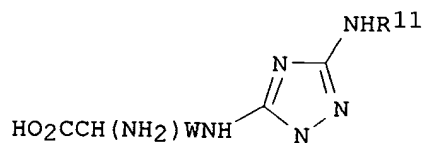
DN 123:56560

IN Hoeger, Carl A.; Rivier, Jean E. F.; Porter, John S.

TI Peptide analogs of **GnRH** containing unnatural amino acids as **GnRH** agonists and antagonists

SO U.S., 21 pp. Cont.-in-part of U.S. 5,296,468.
CODEN: USXXAM

GI



I

- AB Unnatural amino acids are provided which can be incorporated into peptides which either inhibit or promote the secretion of **gonadotropins** by the pituitary gland and inhibit the release of steroids by the gonads. These unnatural amino acids are useful in the synthesis of peptides and have the formula (a): $\text{HO}_2\text{CCH}(\text{NH}_2)\text{WNHC}(\text{:Y})\text{XR}_2$ where W is $(\text{CH}_2)_n$ or $(\text{CH}_2)_j\text{C}_6\text{H}_4\text{-4}$; n is an integer from 1 to 6; j=1,2 or 3, and preferably, Y is N-CN, X is NH and R₂ is alkyl, modified alkyl, alkenyl, alkynyl, aryl or methylpyridyl; or the formula (I): where R₁₁ is H or acyl and W is as defined in (a), and preferably R₁₁ is H and W is $\text{CH}_2\text{C}_6\text{H}_4\text{-4}$. Disclosed are peptides that are analogs of the decapeptide **GnRH** wherein there is at least one residue of an unnatural amino acid in the 3-, 5-, 6- and/or 8-positions. Thus, e.g., peptide Ac-.beta.-D-2NAL-(4Cl)D-Phe-D-3PAL-Ser-AA5-AA6-Leu-AA8-Pro-D-Ala-NH₂ [.beta.-D-2NAL = .beta.-(2-naphthyl)-D-alanine; AA5 = Lys(icg), AA6 = D-Lys(icg), AA8 = ILys; icg = aminoisopropyl cyanoguanidino modified side chain amino group of the amino acid, i.e., (side chain)-NHC(:NCN)NHPr-iso], prepd. by side-chain modification of a resin-bound intermediate, prevented ovulation of female rats at dosages of 1.0-2.5 .mu.g. Pharmaceutical formulations were given.
- TI Peptide analogs of **GnRH** containing unnatural amino acids as **GnRH** agonists and antagonists
- AB Unnatural amino acids are provided which can be incorporated into peptides which either inhibit or promote the secretion of **gonadotropins** by the pituitary gland and inhibit the release of steroids by the gonads. These unnatural amino acids are useful in. . . in (a), and preferably R₁₁ is H and W is $\text{CH}_2\text{C}_6\text{H}_4\text{-4}$. Disclosed are peptides that are analogs of the decapeptide **GnRH** wherein there is at least one residue of an unnatural amino acid in the 3-, 5-, 6- and/or 8-positions. Thus, . . .
- ST peptide unnatural amino acid **GnRH** analog; guanidino amino acid **GnRH** analog; triazole amino acid **GnRH** analog; contraceptive **GnRH** analog unnatural amino acid
- IT Contraceptives
Ovulation
(synthesis of **GnRH** agonists and antagonists contg. unnatural amino acids)
- IT Peptides, preparation
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis of **GnRH** agonists and antagonists contg. unnatural amino acids)
- IT Amino acids, preparation
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(synthesis of **GnRH** agonists and antagonists contg. unnatural amino acids)
- IT
- | | | | |
|---------------------|--------------|--------------|--------------|
| 130883-26-0P | 134457-18-4P | 134457-19-5P | 134457-20-8P |
| 134457-21-9P | 134457-23-1P | 134457-24-2P | 134457-25-3P |
| 134457-26-4P | 134457-27-5P | 134457-28-6P | 134457-29-7P |
| 134457-31-1P | 134457-32-2P | 134457-33-3P | 134457-34-4P |
| 134457-35-5P | 134457-36-6P | 134457-37-7P | 134457-39-9P |
| 134457-41-3P | 134457-54-8P | 134457-58-2P | 134485-03-3P |
| 134981-27-4P | 134981-30-9P | 137280-84-3P | 137280-85-4P |
| 137280-86-5P | 137280-87-6P | 137280-88-7P | 137280-89-8P |

137280-90-1P **137280-91-2P** 137280-92-3P 137280-93-4P
 137280-94-5P 137280-95-6P 137280-97-8P 137280-98-9P
 137280-99-0P 137281-00-6P 137281-01-7P 137281-02-8P
 137305-93-2P 137305-94-3P 137305-95-4P 137305-96-5P
 144744-20-7P 144744-21-8P 144766-12-1P 144766-13-2P
 151336-13-9P **151336-14-0P** 156431-15-1P 156431-16-2P
 156431-17-3P 156431-18-4P 156431-19-5P 156431-20-8P
 156431-21-9P 156431-22-0P 156431-23-1P 156431-24-2P
 156431-25-3P 156431-26-4P 156431-27-5P 156431-28-6P
 156431-29-7P 156431-30-0P 156431-31-1P 156431-34-4P
 156431-35-5P 156431-36-6P 156431-37-7P 156431-38-8P
 156431-39-9P 156431-40-2P 156431-42-4P 156431-43-5P
 156431-44-6P 156431-47-9P 156431-50-4P 156431-51-5P
 156431-55-9P 156431-56-0P 156431-57-1P 156431-58-2P
 156431-60-6P 156431-62-8P 156431-63-9P 156431-64-0P
 156431-66-2P 156431-67-3P 156431-71-9P 156431-72-0P
 156431-73-1P 156431-74-2P 156431-76-4P 156431-77-5P
 156431-78-6P 156431-79-7P 156431-81-1P 156431-83-3P
 156431-84-4P 156431-85-5P 156431-86-6P 156431-87-7P
 156431-89-9P 156431-90-2P **156431-91-3P** 156468-19-8P
 156468-20-1P 156468-21-2P 156468-22-3P 156468-24-5P
 156468-25-6P 156468-27-8P 156468-28-9P 156468-30-3P
 156468-31-4P 156468-32-5P 156468-33-6P 156468-34-7P
 156468-35-8P 156468-36-9P 156468-37-0P 156468-38-1P
 156468-39-2P 156468-40-5P 156468-41-6P 156468-42-7P
 156468-43-8P 156468-44-9P 156468-45-0P 156468-46-1P
 156468-48-3P 156468-49-4P 156468-50-7P 156468-51-8P
 156468-52-9P 156500-23-1P 164332-51-8P 164332-52-9P
 164332-53-0P 164332-54-1P 164332-55-2P 164332-56-3P
 164332-57-4P 164332-58-5P 164332-59-6P 164332-60-9P
 164332-61-0P 164332-62-1P 164332-63-2P 164332-64-3P
 164332-65-4P 164332-66-5P 164332-67-6P 164332-68-7P
 164332-69-8P **164332-70-1P 164332-71-2P**
 164332-72-3P 164332-92-7P

RL: BAC (Biological activity or effector, except adverse); SPN
 (Synthetic preparation); THU (Therapeutic use); BIOL (Biological
 study); PREP (Preparation); USES (Uses)

(synthesis of **GnRH** agonists and antagonists contg.
 unnatural amino acids)

IT 9002-67-9, LH 9002-68-0, FSH 9034-40-6, **GnRH**

RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL
 (Biological study)

(synthesis of **GnRH** agonists and antagonists contg.
 unnatural amino acids)

IT 63-91-2, L-Phenylalanine, reactions 75-31-0, Isopropylamine,
 reactions 673-06-3, D-Phenylalanine 943-80-6 7664-93-9,
 Sulfuric acid, reactions 7697-37-2, Nitric acid, reactions
 7764-95-6 23680-31-1 30135-65-0, Naphthyl isocyanate
 66880-55-5 73259-81-1 76985-10-9 79463-77-7, Diphenyl
 cyanocarbonimide 84624-27-1 102281-45-8 115186-31-7
 125323-99-1 164332-88-1

RL: RCT (Reactant)

(synthesis of **GnRH** agonists and antagonists contg.
 unnatural amino acids)

IT 949-99-5P 33305-77-0P 55533-24-9P 56613-61-7P 61280-75-9P
 137281-03-9DP, MBHA resin bound amide, reaction products
 164332-73-4DP, MBHA resin bound amide, reaction products

M. Borin 08/08/97

164332-74-5DP, MBHA resin bound amide, reaction products
 164332-75-6DP, MBHA resin bound amide, reaction products
164332-76-7DP, MBHA resin bound amide, reaction products
 164332-77-8P 164332-78-9DP, MBHA resin bound amide, reaction
 products 164332-79-0P 164332-80-3P 164332-81-4P 164332-82-5P
 164332-83-6P 164332-84-7P 164332-85-8P 164332-86-9P
 164332-87-0P 164332-89-2P 164332-90-5P 164332-91-6P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
 (synthesis of **GnRH** agonists and antagonists contg.
 unnatural amino acids)

L14 ANSWER 30 OF 59 CAPLUS COPYRIGHT 1997 ACS

AN 1995:32838 CAPLUS

DN 122:106467

AU Janecka, Anna; Janecki, Tomasz; Bowers, Cyril Y.; Folkers, Karl

TI New, highly active antagonists of **LHRH** with acylated
lysine and p-aminophenylalanine in positions 5 and 6

SO Int. J. Pept. Protein Res. (1994), 44(1), 19-23

CODEN: IJPPC3; ISSN: 0367-8377

AB A series of antagonists of the LH releasing hormone (**LHRH**)
 with substitutions in position 5 and/or 6 that included acylated
 lysine or p-aminophenylalanine were synthesized, characterized, and
 tested for antioviulatory activity (AOA) in rats, and histamine
 releasing activity. Some of these antagonists were considerably
 more sol. at neutral pH than antagonists like Antide. Of 37 new
 antagonists, the best physicochem. and biol. properties were found
 for the following two analogs: Ac-D-Nal-D-Cpa-D-Pal-Ser-X-D-Lys(Pic-
 Sar)-Leu-Lys(CHMe2)-Pro-D-Ala-NH2 [I; X = Lys(Pic) (Sartide), Tyr;
 Nal = 3-(2-naphthyl)alanine, Cpa = 3-(4-chlorophenyl)alanine, Pal =
 3-(3-pyridyl)alanine, Pic = picolinoyl]. Both I are sol. in water,
 inhibit ovulation completely at 0.5 .mu.g per rat, and have ED50
 values for histamine release of about 30 .mu.g/mL.

TI New, highly active antagonists of **LHRH** with acylated
 lysine and p-aminophenylalanine in positions 5 and 6

AB A series of antagonists of the LH releasing hormone (**LHRH**)
 with substitutions in position 5 and/or 6 that included acylated
 lysine or p-aminophenylalanine were synthesized, characterized, and
 tested for antioviulatory.

ST **LHRH** antagonist acylllysine analog; aminophenylalanine
 analog **LHRH** antagonist; antioviulatory structure activity
LHRH analog

IT 158276-06-3P 160713-62-2P 160713-63-3P 160713-64-4P
 160713-65-5P 160713-66-6P 160713-67-7P 160713-68-8P
 160713-69-9P 160713-70-2P 160713-71-3P 160713-72-4P
 160713-73-5P 160713-74-6P 160713-75-7P 160713-76-8P
 160713-77-9P 160713-78-0P 160713-80-4P 160713-81-5P
 160713-82-6P 160713-83-7P **160713-85-9P**
160713-87-1P 160713-88-2P 160713-89-3P 160713-93-9P
 160713-94-0P 160713-95-1P 160713-96-2P

RL: SPN (Synthetic preparation); PREP (Preparation)
 (prepn. and antioviulatory activity of)

IT **160713-86-0P**

RL: SPN (Synthetic preparation); PREP (Preparation)
 (prepn., soly., and antioviulatory activity of)

IT 33515-09-2DP, Synthetic LH-RH, acylated lysine and
 aminophenylalanine analogs 112481-36-4DP, acylated lysine and
 aminophenylalanine analogs 160713-79-1P **160713-84-8P**

M. Borin 08/08/97

160825-64-9P, Sartide

RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn., soly., antiovolatory activity, and histamine releasing activity of)

- L14 ANSWER 45 OF 59 CAPLUS COPYRIGHT 1997 ACS
AN 1993:1068 CAPLUS
DN 118:1068
AU Rivier, Jean; Porter, John; Hoeger, Carl; Theobald, Paula; Craig, A. Grey; Dykert, John; Corrigan, Anne; Perrin, Marilyn; Hook, William A.; et al.
- TI **Gonadotropin**-releasing hormone antagonists with N.omega.-triazolylornithine, -lysine, or -p-aminophenylalanine residues at positions 5 and 6
SO J. Med. Chem. (1992), 35(23), 4270-8
CODEN: JMCMAR; ISSN: 0022-2623
- AB In order to be used as fertility regulators in humans, **gonadotropin** releasing hormone (**GnRH**) antagonists must be extremely potent and long acting, and exhibit negligible side effects such as stimulating histamine release. To this aim, we have recently synthesized a series of analogs with the std. Ac-D-Nal1-D-Cpa2-D-Pal3 [Nal = 3-(2-naphthyl)alanine, Cpa = 4-chlorophenylalanine, Pal = 3-(3-pyridyl)alanine] substitutions, where the N.omega.-amino function of ornithine, lysine, or p-aminophenylalanine (Aph) was converted to the aminotriazolyl (Atz) derivs. at positions 5 and 6 with further modifications at positions 7 and 10. The analogs were tested for their ability to bind to pituitary cell membranes, to release histamine in a mast cell assay, to inhibit LH secretion by castrated male rats or cultured pituitary cells, and to interfere with the ovulation in intact female rats. While the s.c. injection of 50 .mu.g of Azaline A, [Ac-D-Nal1,D-Cpa2,D-Pal1,Lys5(Atz),D-Lys6(Atz),ILys8,D-Ala10] **GnRH** (ILys = N.epsilon.-isopropyllysine), dissolved in 0.2 mL of an aq. media significantly inhibited LH release in the castrated male rat for 24 h, the same dose of Azaline B, [Ac-D-Nal1,D-Cpa2,D-Pal3,Aph5(Atz),D-Aph6(Atz),ILys8,D-Ala10] **GnRH**, inhibited LH release for 72 h. A similar long duration of action was obsd. for Antide, [Ac-D-Nal1,D-Cpa2,D-Pal3,Lys5(Nic),D-Lys6(Nic),ILys8,D-Ala10] **GnRH** (Nic = nicotinoyl). In the same paradigm, a 5-fold diln. of the peptide (50 .mu.g in 1 mL) and the use of three injection sites rather than one resulted in significantly shorter duration of action for most of the peptides tested.
- TI **Gonadotropin**-releasing hormone antagonists with N.omega.-triazolylornithine, -lysine, or -p-aminophenylalanine residues at positions 5 and 6
- AB In order to be used as fertility regulators in humans, **gonadotropin** releasing hormone (**GnRH**) antagonists must be extremely potent and long acting, and exhibit negligible side effects such as stimulating histamine release. To this. . . and to interfere with the ovulation in intact female rats. While the s.c. injection of 50 .mu.g of Azaline A, [Ac-D-Nal1,D-Cpa2,D-Pal1,Lys5(Atz),D-Lys6(Atz),ILys8,D-Ala10] **GnRH** (ILys = N.epsilon.-isopropyllysine), dissolved in 0.2 mL of an aq. media significantly inhibited LH release in the castrated male rat for 24 h, the same dose of Azaline B, [Ac-D-Nal1,D-Cpa2,D-Pal3,Aph5(Atz),D-Aph6(Atz),ILys8,D-Ala10] **GnRH**, inhibited LH release for 72

- h. A similar long duration of action was obsd. for Antide,
[Ac-D-Nal1,D-Cpa2,D-Pal3,Lys5(Nic),D-Lys6(Nic),ILys8,D-Ala10]
GnRH (Nic = nicotinoyl). In the same paradigm, a 5-fold
diln. of the peptide (50 .mu.g in 1 mL) and the. . .
- ST **gonadotropin** releasing hormone antagonist; LH release
inhibition **gonadotropin** releasing hormone
- IT Molecular structure-biological activity relationship
(LH release-inhibiting, of **gonadotropin**-releasing
hormone analogs)
- IT 9034-40-6, **Gonadotropin**-releasing hormone
RL: BIOL (Biological study)
(antagonists, peptide analogs as)
- IT 101685-06-7 103733-02-4 120287-85-6 124904-93-4 134457-26-4
134457-27-5 134457-28-6 **134457-56-0 135215-95-1**
144744-18-3 144744-20-7 144744-21-8 144744-22-9 144766-12-1
144766-13-2
RL: BIOL (Biological study)
(as **gonadotropin**-releasing hormone antagonist)
- IT 112568-12-4P 144744-19-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as **gonadotropin**-releasing hormone
antagonist)
- IT 9002-67-9, **Luteinizing** hormone
RL: BIOL (Biological study)
(release of, **gonadotropin**-releasing hormone analogs for
inhibition of)
- L14 ANSWER 50 OF 59 CAPLUS COPYRIGHT 1997 ACS
AN 1991:240782 CAPLUS
DN 114:240782
- AU Nestor, J. J., Jr.; Tahilramani, R.; Ho, T. L.; Goodpasture, J. C.;
Vickery, B. H.; Ferrandon, P.
- TI Design of **luteinizing** hormone releasing hormone
antagonists with reduced potential for side effects
- SO Pept., Proc. Eur. Pept. Symp., 20th (1989), Meeting Date 1988,
592-4. Editor(s): Jung, Guenther; Bayer, Ernst. Publisher: de
Gruyter, Berlin, Fed. Rep. Ger.
CODEN: 57ACAI
- AB A report from a symposium on the antiovolatory and mast cell
degranulating activities of D-Ng,Ng'-dialkylhomoarginine derivs. of
LH-RH antagonists. Detirelix analogs Ac-D-Nal-D-Phe(p-Cl)-D-Pal-Ser-
Tyr-X-Leu-hArg(Et)2-Pro-D-Ala-NH2 [I; Nal = 3-(2-naphthyl)alanine,
Pal = 3-(3-pyridyl)alanine, hArg(Et)2 = Ng,Ng'-diethylhomoarginine;
X = D-Pal, D-hArg(Et)2] had 6-8-fold improved antagonistic potency
compared to detirelix, and a 70-1000-fold decrease in toxicity. I
[X = D-hArg(Et)2] was selected for clin. trials.
- TI Design of **luteinizing** hormone releasing hormone
antagonists with reduced potential for side effects
- IT 89662-30-6D, Detirelix, dialkylhomoarginine analogs 120128-39-4
120128-56-5 124904-93-4 124926-38-1 133951-43-6
133951-44-7 133951-45-8 133972-58-4
RL: BIOL (Biological study)
(antiovolatory and mast cell degranulation activities of)
- L14 ANSWER 58 OF 59 CAPLUS COPYRIGHT 1997 ACS
AN 1987:131868 CAPLUS
DN 106:131868

- AU Folkers, Karl; Bowers, Cyril; Tang, Pui Fun L.; Kobota, Minoru; Xiao, Shao Bo; Bender, Wolfgang; Liu, Yin Zeng
- TI Relative potencies of antagonists of the **luteinizing** hormone releasing hormone with Lys8 and Arg8 and substitutions in positions 3,5,6,7 and 8
- SO Z. Naturforsch., C: Biosci. (1986), 41(11-12), 1087-91
CODEN: ZNCBDA; ISSN: 0341-0382
- AB Antagonists of **LHRH** [9034-40-6] of increased potency is a goal for control of ovulation. In the design and synthesis of 26 decapeptides, emphasis was given to analogs with Lys8 and Arg8 and with various substitutions in positions 3, 5, 6, 7, and 8. Two antagonists, [N-Ac-D-2-Nal1,D-pClPhe2,D-3-Pal3,Ser4,Tyr5,D-Arg6,Leu7,Lys8,Pro9,D-Ala10]-NH2 [**107348-19-6**] and [N-Ac-wyd-2-Nal1,D-pClPhe2,D-3-Pal3,Ser4,Arg5,D-3-Pal6,Leu7,Arg8,Pro9,D-Ala10]-NH2 [101685-06-7] showed 80-85% antiovaratory activity (AOA) at 0.25 .mu.g in the rat. The latter antagonist showed 60% AOA at 0.125 .mu.g. Of 4 pairs of analogs with Arg8 and Lys8, resp., 2 pairs favored Lys8 over Arg8 for potency. One pair showed negligible difference and another pair favored Arg8 over Lys8. There is specificity of substitution for potency. In other antagonists, D-3-Pal3,Tyr5 or Phe5,D-Arg6 and Leu7 or Nle7 or Val7 and Arg8 were variously effective substitutions for increase of potency and redn. of histamine release.
- TI Relative potencies of antagonists of the **luteinizing** hormone releasing hormone with Lys8 and Arg8 and substitutions in positions 3,5,6,7 and 8
- AB Antagonists of **LHRH** [9034-40-6] of increased potency is a goal for control of ovulation. In the design and synthesis of 26 decapeptides, emphasis. . . analogs with Lys8 and Arg8 and with various substitutions in positions 3, 5, 6, 7, and 8. Two antagonists, [N-Ac-D-2-Nal1,D-pClPhe2,D-3-Pal3,Ser4,Tyr5,D-Arg6,Leu7,Lys8,Pro9,D-Ala10]-NH2 [**107348-19-6**] and [N-Ac-wyd-2-Nal1,D-pClPhe2,D-3-Pal3,Ser4,Arg5,D-3-Pal6,Leu7,Arg8,Pro9,D-Ala10]-NH2 [101685-06-7] showed 80-85% antiovaratory activity (AOA) at 0.25 .mu.g in the rat. The latter antagonist showed 60% AOA. . .
- ST **LHRH** antagonist peptide structure activity; ovulation inhibitor **LHRH** antagonist structure
- IT 9034-40-6, **LHRH**
RL: BIOL (Biological study)
(antagonist, antihistaminic and ovulation-inhibiting activity of, mol. structure in relation to)
- IT 93128-18-8 101685-06-7 103974-88-5 107348-04-9 107348-05-0
107348-06-1 107348-07-2 107348-08-3 107348-09-4 107348-10-7
107348-11-8 107348-12-9 107348-13-0 107348-14-1 107348-15-2
107348-16-3 **107348-17-4** 107348-18-5 **107348-19-6**
107375-97-3 107375-98-4 107375-99-5 107376-00-1 107376-01-2
107376-02-3
RL: BIOL (Biological study)
(ovulation-inhibiting activity of, mol. structure in relation to)

=> d au,so 24,25,29,30,45,50,58

SO PCT Int. Appl., 86 pp.
CODEN: PIXXD2

L14 ANSWER 25 OF 59 CAPLUS COPYRIGHT 1997 ACS
IN Haviv, Fortuna; Greer, Jonathan; Swenson, Rolf E.; Sauer, Daryl R.
SO PCT Int. Appl., 60 pp.
CODEN: PIXXD2

L14 ANSWER 29 OF 59 CAPLUS COPYRIGHT 1997 ACS
IN Hoeger, Carl A.; Rivier, Jean E. F.; Porter, John S.
SO U.S., 21 pp. Cont.-in-part of U.S. 5,296,468.
CODEN: USXXAM

L14 ANSWER 30 OF 59 CAPLUS COPYRIGHT 1997 ACS
AU Janecka, Anna; Janecki, Tomasz; Bowers, Cyril Y.; Folkers, Karl
SO Int. J. Pept. Protein Res. (1994), 44(1), 19-23
CODEN: IJPPC3; ISSN: 0367-8377

L14 ANSWER 45 OF 59 CAPLUS COPYRIGHT 1997 ACS
AU Rivier, Jean; Porter, John; Hoeger, Carl; Theobald, Paula; Craig, A.
Grey; Dykert, John; Corrigan, Anne; Perrin, Marilyn; Hook, William
A.; et al.
SO J. Med. Chem. (1992), 35(23), 4270-8
CODEN: JMCMAR; ISSN: 0022-2623

L14 ANSWER 50 OF 59 CAPLUS COPYRIGHT 1997 ACS
AU Nestor, J. J., Jr.; Tahilramani, R.; Ho, T. L.; Goodpasture, J. C.;
Vickery, B. H.; Ferrandon, P.
SO Pept., Proc. Eur. Pept. Symp., 20th (1989), Meeting Date 1988,
592-4. Editor(s): Jung, Guenther; Bayer, Ernst. Publisher: de
Gruyter, Berlin, Fed. Rep. Ger.
CODEN: 57ACAI

L14 ANSWER 58 OF 59 CAPLUS COPYRIGHT 1997 ACS
AU Folkers, Karl; Bowers, Cyril; Tang, Pui Fun L.; Kobota, Minoru;
Xiao, Shao Bo; Bender, Wolfgang; Liu, Yin Zeng
SO Z. Naturforsch., C: Biosci. (1986), 41(11-12), 1087-91
CODEN: ZNCBDA; ISSN: 0341-0382

=> d au,so,pi,pa,prai 24,25,29,30,45,50,58

L14 ANSWER 24 OF 59 CAPLUS COPYRIGHT 1997 ACS
IN Greer, Jonathan; Haviv, Fortuna; Fitzpatrick, Timothy D.; Swenson,
Rolf E.; Nichols, Charles J.; Mort, Nicholas A.
SO PCT Int. Appl., 86 pp.
CODEN: PIXXD2
PI WO 9413313 A1 940623
PA Abbott Laboratories, USA
PRAI US 92-987921 921204

L14 ANSWER 25 OF 59 CAPLUS COPYRIGHT 1997 ACS
IN Haviv, Fortuna; Greer, Jonathan; Swenson, Rolf E.; Sauer, Daryl R.
SO PCT Int. Appl., 60 pp.
CODEN: PIXXD2
PI WO 9414841 A1 940707
PA Abbott Laboratories, USA

PRAI US 92-993202 921218

L14 ANSWER 29 OF 59 CAPLUS COPYRIGHT 1997 ACS
 IN Hoeger, Carl A.; Rivier, Jean E. F.; Porter, John S.
 SO U.S., 21 pp. Cont.-in-part of U.S. 5,296,468.
 CODEN: USXXAM
 PI US 5352796 A 941004
 PA Salk Institute For Biological Studies, USA
 PRAI US 89-428827 891030
 US 90-545239 900627
 US 91-669695 910314
 US 93-6729 930121

L14 ANSWER 30 OF 59 CAPLUS COPYRIGHT 1997 ACS
 AU Janecka, Anna; Janecki, Tomasz; Bowers, Cyril Y.; Folkers, Karl
 SO Int. J. Pept. Protein Res. (1994), 44(1), 19-23
 CODEN: IJPPC3; ISSN: 0367-8377

L14 ANSWER 45 OF 59 CAPLUS COPYRIGHT 1997 ACS
 AU Rivier, Jean; Porter, John; Hoeger, Carl; Theobald, Paula; Craig, A.
 Grey; Dykert, John; Corrigan, Anne; Perrin, Marilyn; Hook, William
 A.; et al.
 SO J. Med. Chem. (1992), 35(23), 4270-8
 CODEN: JMCMAR; ISSN: 0022-2623

L14 ANSWER 50 OF 59 CAPLUS COPYRIGHT 1997 ACS
 AU Nestor, J. J., Jr.; Tahilramani, R.; Ho, T. L.; Goodpasture, J. C.;
 Vickery, B. H.; Ferrandon, P.
 SO Pept., Proc. Eur. Pept. Symp., 20th (1989), Meeting Date 1988,
 592-4. Editor(s): Jung, Guenther; Bayer, Ernst. Publisher: de
 Gruyter, Berlin, Fed. Rep. Ger.
 CODEN: 57ACAI

L14 ANSWER 58 OF 59 CAPLUS COPYRIGHT 1997 ACS
 AU Folkers, Karl; Bowers, Cyril; Tang, Pui Fun L.; Kobota, Minoru;
 Xiao, Shao Bo; Bender, Wolfgang; Liu, Yin Zeng
 SO Z. Naturforsch., C: Biosci. (1986), 41(11-12), 1087-91
 CODEN: ZNCBDA; ISSN: 0341-0382

=> d an,au,ti,so,pi,prai,an,abs,kwic 16-18,20,21,23,40,43,44,47,48,50

L14 ANSWER 16 OF 59 CAPLUS COPYRIGHT 1997 ACS
 AN 1996:13304 CAPLUS
 DN 124:203099
 IN Folkers, Karl A.; Ljungqvist, Anders; Feng, Dong Mei; Kubota,
 Minoru; Tang, Pui Fun L.; Bowers, Cyril Y.
 TI Preparation of peptide analog **LHRH** antagonists with low
 histamine release.
 SO U.S., 20 pp. Cont.-in-part of U.S. 4,935,491.
 CODEN: USXXAM
 PI US 5470947 A 951128
 PRAI US 87-88431 870824
 AN 1996:13304 CAPLUS
 DN 124:203099
 AB AA1-D-pClPhe-D-3Pal-Ser-AA5-AA6-AA7-AA8-Pro-D-Ala-NH2 [AA1 =
 Ac-D-2Nal, D-pClPhe, D-Cl2Phe; AA5 = Tyr, NicLys, PicLys, MNicLys,
 M. Borin 08/08/97

MPicLys, INicLys, DMGLys, PzcLys, c-PzACAla; AA6 = D-NicLys, D-PicLys, D-MNicLys, D-MPicLys, D-INicLys, D-BzLys, ~~D-PzLys, D-PzACAla, D-NACAla, D-PACAla~~, AA7 = Leu, Aile, Nle, Val, NVal, Abu, Ala; AA8 = ILys, IOrn; MNLys = NE -(6-methylnicotinoyl)lysine; MPicLys = NE -(6-methylpicolinoyl)lysine; NACAla = 3(4-nicotinoylaminocyclohexyl)alanine; 2-Nal = 3-(2-naphthyl)alanine; NicLys = NE -nicotinoyllysine; NicOrn = Nd -nicotinoylornithine; Nle = norleucine; NMeLeu = N-methyllleucine; Nval = norvaline; PACAla = 3(4-picolinoylaminocyclohexyl)alanine; 3-Pal = 3-(3-pyridyl)alanine; pClPhe = 3-(4-chloro)phenylalanine; PicLys = NE -picolinoyllysine; Pip = piperidine-2-carboxylic acid; PmcLys = NE -(4-pyrimidinylcarbonyl)lysine; PmACAla = 3[4(4-pyrimidinylcarbonyl)aminocyclohexyl]alanine; PzACAla = 3(4-pyrazinylcarbonylaminocyclohexyl)alanine; 3-PzAla = 3-pyrazinylalanine; PzcLys = NE -pyrazinylcarbonyllysine; INicLys = NE -isonicotinoyllysine; DMGLys = NE -(N,N-dimethylglycyl)lysine; Aile = alloseucine; Abu = 2-aminobutyric acid; ILys = NE -isopropyllysine; IOrn = Nd-isopropylornithine], and other Antide-related peptides, were prepd. Ac-D-2-Nal-D-pClPhe-D-3-Pal-Ser-PicLys-cis-DpZACAla-Leu-ILys-Pro-D-Ala-NH₂ was one of the most potent and had higher antiovolatory activity than Antide, i.e. 73%/0.25 .mu.g and 100%/0.5 .mu.g vs. 36%/0.5 .mu.g and 100%/1.0 .mu.g. Antide showed significant (p<0.001) duration of action when injected at 10 ug 44 h before 50 ng of the agonist [D-3-Qal6]-LHRH. Antide showed oral AOA at 600 ug (73%) and at 1200 ug (100%) with negligible difference being found between water and corn oil oral formulations.

- TI Preparation of peptide analog **LHRH** antagonists with low histamine release.
- AB . . . Antide showed significant (p<0.001) duration of action when injected at 10 ug 44 h before 50 ng of the agonist [D-3-Qal6]-LHRH. Antide showed oral AOA at 600 ug (73%) and at 1200 ug (100%) with negligible difference being found between water. . .
- ST peptide prepn **LHRH** antagonist prepn; antide analog prepn **LHRH** antagonist; antiovolatory peptide prepn
- IT Ovulation
(inhibitors; prepn. of peptide analog **LHRH** antagonists with low histamine release)
- IT Molecular structure-biological activity relationship
(of peptide analog **LHRH** antagonists with low histamine release)
- IT Peptides, preparation
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of peptide analog **LHRH** antagonists with low histamine release)
- IT 9034-40-6, **LHRH**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antagonists; prepn. of peptide analog **LHRH** antagonists with low histamine release)
- IT 118992-93-1P 174397-21-8P 174397-22-9P 174397-23-0P
174397-24-1P 174397-25-2P 174397-26-3P 174397-27-4P
174397-28-5P 174397-29-6P 174397-30-9P 174397-31-0P
174397-32-1P 174397-33-2P 174397-34-3P 174397-35-4P
174397-36-5P 174397-37-6P 174397-38-7P 174397-39-8P
174397-40-1P 174397-41-2P 174397-42-3P 174397-43-4P

174397-44-5P 174397-45-6P 174397-46-7P **174397-47-8P**
 174397-48-9P **174397-49-0P** 174397-50-3P 174397-51-4P
 174512-00-6P

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of peptide analog **LHRH** antagonists with low histamine release)

IT 59-67-6, 3-Pyridinecarboxylic acid, reactions 79-04-9, Chloroacetyl chloride 98-97-5, Pyrazinecarboxylic acid 98-98-6, Picolinic acid 100-02-7, reactions 104-94-9, p-Anisidine 120-92-3, Cyclopentanone 123-54-6, Acetylacetone, reactions 124-40-3, reactions 1119-34-2, Arginine hydrochloride 2389-45-9, BOC-Lys(Z)-OH 2480-93-5 3222-47-7, 6-MethylNicotinic acid 13734-28-6 21887-64-9 34404-30-3 98500-77-7 106719-44-2 122566-51-2 132695-92-2

RL: RCT (Reactant)

(prepn. of peptide analog **LHRH** antagonists with low histamine release)

IT 2882-35-1P, p-Nitrophenyl isonicotinate 14609-04-2P 20088-23-7P, Pyrazinecarboxylic acid p-nitrophenylester 24690-42-4P, p-Nitrophenyl nicotinate 65671-53-6P 74104-89-5P, P-Nitrophenyl picolinate 122532-77-8P 122532-78-9P 122532-79-0P 122532-80-3P 122532-81-4P 122532-82-5P 122532-83-6P 122532-84-7P 122532-85-8P 122532-86-9P 122532-87-0P 122532-88-1P 122532-89-2P 122532-90-5P 122532-91-6P 122532-92-7P 122532-93-8P 122532-95-0P, p-Nitrophenyl 6-methylnicotinate 122546-52-5P 122566-50-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)

(prepn. of peptide analog **LHRH** antagonists with low histamine release)

L14 ANSWER 17 OF 59 CAPLUS COPYRIGHT 1997 ACS

AN 1995:818569 CAPLUS

DN 123:228905

IN Haviv, Fortuna; Fitzpatrick, Timothy D.; Swenson, Rolf E.; Nichols, Charles J.; Mort, Nicholas A.

TI Preparation of N-terminus acylated analogs of **LHRH** as **LHRH** antagonists.

SO PCT Int. Appl., 91 pp.
 CODEN: PIXXD2

PI WO 9504541 A1 950216

PRAI US 93-103022 930806

US 94-279677 940727

AN 1995:818569 CAPLUS

DN 123:228905

AB X-A-B-C-D-E-F-G-H-I-J-K [X = shikimyl, dihydroshikimyl, picolinoyl, salicyl, p-toluenesulfonyl, furoyl, tetrahydrofuroyl, thienylcarbonyl, tetrahydrothienylcarbonyl, pyrrolylcarbonyl, prolyl, N-acetylprolyl, (alkyl-substituted) nicotinoyl, isonicotinoyl, quinolinecarbonyl, etc.; A = null, D-Ala, 3-aminopropionyl, 7-aminoheptanoyl, 11-aminoundecanoyl, azaglycyl, Gly, sarcosyl, D-Ser, etc.; B = D-Phe, D-3-(4-chlorophenyl)alanyl, Gly, azaglycyl, D-3-(naphth-2-yl)alanyl, etc.; C = D-3,3-diphenylalanyl, D-3-(4-fluorophenyl)alanyl, D-3-(quinolin-3-yl)alanyl, etc.; D = D-Ala, Gly, D-3-(naphth-1-yl)alanyl, D-3-(pyrid-3-yl)alanyl,

M. Borin 08/08/97

D-3-(thiazol-2-yl)alanyl, etc.; E = Gly, Ser, homoseryl, etc.; F = (N.alpha.-alkyl-substituted) Ala, 3-(4-nitrophenyl)alanyl, 3-(4-aminocyclohexyl)alanyl, Tyr, Phe, Arg, Gly, His, etc.; G = Gly, D-citrullyl, D-homocitrullyl, .beta.-alanyl, etc.; H = Leu, Gly, Val, Pro, sarcosyl, cyclohexylalanyl, etc.; I = citrullyl, homocitrullyl, His, Arg, homoarginyl, etc.; J = Pro, 4-hydroxyprolyl, pipecolyl, azetidyl, 2,8-tetrahydroisoquinolin-2-carbonyl, sarcosyl, Gly, etc.; K = NHet, D-Ala-OH, D-Ala-NH₂, Glu-OH, D-Ser-NH₂, azaglycylamide, etc.], were prepd. Thus, 2-furoyl-Gly-D-2-Nal-D-4-Cl-Phe-D-3-Pal-Ser-NMeTyr-D-Lys(Shik)-Leu-Harg-Pro-D-Ala-NH₂[Harg = homoarginyl, D-Lys(Shik) = D-Lys acylated at N.epsilon. by shikimyl, D-2-Nal = D-3-naphth-2-ylalanyl, D-3-Pal = 3-pyrid-3-ylalanyl, D-4-Cl-Phe = D-3-(4-chlorophenyl)alanyl, NMeTyr = N.alpha.-methylated Tyr], prepd. by solid phase synthesis, antagonized **LHRH** with pA₂ = 11.77 according to the method of F. Haviv.

TI Preparation of N-terminus acylated analogs of **LHRH** as **LHRH** antagonists.

AB . . . by shikimyl, D-2-Nal = D-3-naphth-2-ylalanyl, D-3-Pal = 3-pyrid-3-ylalanyl, D-4-Cl-Phe = D-3-(4-chlorophenyl)alanyl, NMeTyr = N.alpha.-methylated Tyr], prepd. by solid phase synthesis, antagonized **LHRH** with pA₂ = 11.77 according to the method of F. Haviv.

ST peptide analog prepn **LHRH** antagonist; sex hormone suppression peptide **LHRH** antagonist

IT Peptides, preparation

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of N-terminus acylated analogs of **LHRH** as **LHRH** antagonists)

IT Hormones

RL: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)

(sex, suppressors; prepn. of N-terminus acylated analogs of **LHRH** as **LHRH** antagonists)

IT	157147-52-9P	168192-25-4P	168192-26-5P	168192-27-6P
	168192-28-7P	168192-29-8P	168192-30-1P	168192-31-2P
	168192-32-3P	168192-33-4P	168192-34-5P	168192-35-6P
	168192-36-7P	168192-37-8P	168192-38-9P	168192-39-0P
	168192-40-3P	168192-41-4P	168192-42-5P	168192-43-6P
	168192-44-7P	168192-45-8P	168192-46-9P	168192-47-0P
	168192-48-1P	168192-49-2P	168192-51-6P	168192-53-8P
	168192-55-0P	168192-57-2P	168192-59-4P	168192-61-8P
	168192-63-0P	168192-65-2P	168192-67-4P	168192-69-6P
	168192-71-0P	168192-73-2P	168192-75-4P	168192-77-6P
	168192-79-8P	168192-80-1P	168192-81-2P	168192-83-4P
	168192-85-6P	168192-87-8P	168192-89-0P	168192-91-4P
	168192-92-5P	168192-93-6P	168192-94-7P	168192-95-8P
	168192-96-9P	168192-97-0P	168192-98-1P	168192-99-2P
	168193-00-8P	168193-01-9P	168193-02-0P	168193-03-1P
	168193-04-2P	168193-05-3P	168193-06-4P	168193-07-5P
	168193-08-6P	168193-09-7P	168193-10-0P	168193-11-1P
	168193-12-2P	168193-13-3P	168193-14-4P	168193-15-5P
	168193-16-6P	168193-17-7P	168193-18-8P	168193-19-9P
	168193-20-2P	168193-21-3P	168193-22-4P	
	168193-23-5P	168193-24-6P	168193-25-7P	168193-26-8P

168193-27-9P 168193-28-0P 168193-29-1P 168193-30-4P
168193-31-5P 168193-32-6P 168193-33-7P
168193-34-8P 168193-35-9P 168193-36-0P
 168193-37-1P 168193-38-2P **168193-39-3P**
168193-40-6P 168193-41-7P 168193-42-8P
168193-43-9P 168193-44-0P 168193-45-1P
168193-46-2P 168193-47-3P 168193-48-4P
168193-49-5P 168193-50-8P 168193-51-9P
168193-52-0P 168193-53-1P 168193-54-2P 168193-55-3P
 168193-56-4P 168193-57-5P 168193-58-6P 168193-59-7P
 168193-60-0P 168193-62-2P 168193-63-3P 168193-64-4P
 168193-66-6P 168193-68-8P 168193-70-2P 168193-72-4P
 168193-74-6P 168193-76-8P 168193-78-0P 168193-80-4P
 168193-82-6P 168193-84-8P 168193-86-0P **168193-87-1P**
 168193-88-2P 168193-89-3P 168193-90-6P 168193-91-7P
 168193-92-8P 168193-93-9P 168193-94-0P 168193-95-1P
 168193-96-2P 168193-98-4P 168394-96-5P **168394-97-6P**
168394-98-7P 168394-99-8P 168395-00-4P 168395-02-6P
 168395-04-8P 168395-06-0P 168395-08-2P 168395-10-6P
 168395-12-8P 168395-14-0P 168395-16-2P 168395-18-4P
 168395-20-8P 168395-21-9P 168395-22-0P 168395-23-1P
 168395-24-2P 168395-25-3P 168607-89-4P 168607-90-7P
 168607-91-8P 168607-92-9P

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of N-terminus acylated analogs of **LHRH** as **LHRH** antagonists)

IT 9034-40-6, **LHRH**

RL: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)

(prepn. of N-terminus acylated analogs of **LHRH** as **LHRH** antagonists)

IT 59-67-6, Nicotinic acid, reactions 98-59-9, p-Toluenesulfonyl chloride 138-59-0, Shikimic acid 553-53-7, Nicotinic acid hydrazide 2188-18-3 3303-84-2, N-tert-Butoxycarbonyl-3-aminopropionic acid 3326-71-4, 2-Furoic acid hydrazide 4530-20-5 6404-29-1 7764-95-6D, resin bound 13139-15-6 13139-16-7 13734-36-6 13836-37-8 14609-04-2 15761-39-4 16874-33-2, Tetrahydro-2-furoic acid 16937-99-8 18942-49-9 23680-31-1 28968-64-1 35320-22-0D, H-D-Ala-NH₂, resin bound 37553-65-4 37784-17-1 40298-71-3 47173-80-8 51077-14-6 53363-89-6 57292-44-1 57294-38-9, N-tert-Butoxycarbonyl-.gamma.-aminobutyric acid 57817-43-3 58438-04-3 60142-89-4 66838-42-4 68090-88-0 69541-62-4 76932-48-4 76985-10-9 87392-05-0 87392-07-2 94849-39-5D, resin bound 98266-33-2 110115-45-2 115186-31-7 117142-26-4 121080-95-3 121080-97-5 122546-52-5 125323-99-1 135101-22-3 156706-55-7 168193-97-3 168395-26-4

RL: RCT (Reactant)

(prepn. of N-terminus acylated analogs of **LHRH** as **LHRH** antagonists)

L14 ANSWER 18 OF 59 CAPLUS COPYRIGHT 1997 ACS

AN 1995:812789 CAPLUS

DN 123:228906

IN Haviv, Fortuna; Fitzpatrick, Timothy D.; Swenson, Rolf E.; Nichols, Charles J.; Mort, Nicholas A.

TI Preparation of N-terminus modified analogs of **luteinizing**
 hormone-releasing hormone (**LHRH**)
 SO PCT Int. Appl., 42 pp.
 CODEN: PIXXD2
 PI WO 9504540 A1 950216
 PRAI US 93-103022 930806
 AN 1995:812789 CAPLUS
 DN 123:228906
 AB N-acyldecapeptides X-A-B-C-D-E-F-G-H-I-J [I; X = acyl; A = D-Phe,
 D-4-ClPhe, D-4-FPhe, D-3-(quinolin-3-yl)alanine, Sar, Gly, etc.; B =
 D-4-ClPhe, D-3,3-diphenylalanine, D-4-FPhe, D-3-(naphth-2-
 yl)alanine, D-Phe, D-3-(quinolin-3-yl)alanine; C = D-Ala,
 D-3-(benzo[b]thien-2-yl)alanine, Gly, D-3-(naphth-2-yl)alanine,
 D-3-(pyrid-3-yl)alanine, D-3-(quinolin-3-yl)alanine,
 D-3-(thiazol-2-yl)alanine; D = Gly, Ser, homo-Ser, Ser(CH₂Ph),
 N.alpha.-C1-4 alkylserine; E = N.alpha.-R-3-R₂-Ala,
 N.alpha.-R-3-R₃-Lys, N.alpha.-R-Tyr, N.alpha.-R-Tyr(Me),
 N.alpha.-R-Phe, N.alpha.-cyclohexylalanine, N.alpha.-R-Gly,
 N.alpha.-R-Arg, N.alpha.-R1-His or -homo-His; wherein R = H, C1-4
 alkyl; R₂ = 4-(3-amino-1,2,4-triazol-5-yl)aminophenyl,
 4-[(3-amino-1,2,4-triazol-5-yl)amino]methylphenyl,
 4-(nicotinylamino)cyclohexyl, 4-nitrophenyl, 4-aminophenyl, etc.; R₃
 = N.epsilon.-nicotinyl or 3-amino-1,2,4-triazol-5-yl; F = Gly,
 .beta.-alanine, ~~D-citrulline, D-homo-citrulline, etc.~~ G =
 N.alpha.-R₄-Leu, Gly, Sar, Pro, Val, N.alpha.-R₄-L-
 cyclohexylalanine; R₄ = H, C1-6 alkyl; H = L-citrulline,
 L-homo-citrulline, His, Lys(iso-Pr), N.alpha.-R₄-Arg (wherein = same
 as above), homo-Arg, etc.; I = Pro, 4-hydroxy-L-proline,
 L-pipecoline, L-azetidine, N.alpha.-R₄-Leu (wherein R₄ = same as
 above), Sar, Gly, N.alpha.-R₄-Ala, etc.; J = NH₂Et, N.alpha.-R₄-D- or
 -L-Ala-NH₂ (R₄ = same as above), D-Ala-OH, D- or L-Glu, Sar-NH₂,
 D-Ser-NH₂, azaglycine, Gly-NH₂] are prepd. These peptides I are
 potent antagonists of **LHRH** and are useful for suppressing
 the levels of sex hormones in mammals. Thus, CHO-D-2Nal-D-4-ClPhe-D-
 3Pal-Ser-MeTyr-D-Lys(Nic)-Leu-Lys(iso-Pr)-Pro-D-Ala-NH₂ [2Nal =
 3-(naphth-2-yl)alanine; 4-ClPhe = 3-(4-chlorophenyl)alanine, 3Pal =
 3-(pyrid-3-yl)alanine, Nic = nicotinyl] was prepd. by a
 Milligen-Bioscience 9,500 peptide synthesizer, involving sequential
 coupling of N-Boc-protected amino acids Boc-Pro-OH,
 Boc-Lys(Cbz,iso-Pr)-OH, Boc-Leu-OH, Boc-D-Lys(Nic)-OH,
 Boc-MeTyr(2,6-diCl-Bzl)-OH, Boc-Ser(Bzl)-OH, Boc-D-3Pal-OH,
 Boc-D-4ClPhe-OH, Boc-D-2Nal-OH and formic acid on a D-Ala-NH-resin
 (4-methylbenzhydrylamine resin). A total of 27 I were prepd. and in
 vitro showed pA₂ values 8.8-11.46 in a test for **LHRH**
 antagonist potency, wherein the value of pA₂ is the neg. logarithm
 of the concn. of the particular antagonist test compd. required to
 shift the response curve produced by the agonist leuprolide to
 two-fold higher concn. and typically pA₂ values of .gtoreq.9.5 are
 indicative of good **LHRH** antagonist activity, with values
 of .gtoreq.10.0 being preferred. MeCH₂CO-D-2Nal-D-4ClPhe-D-3Pal-Ser-
 MeTyr-D-Cit-Leu-Arg-Pro-D-Ala-NH₂ (Cit = citrulline) showed the
 highest pA₂ value (11.46).
 TI Preparation of N-terminus modified analogs of **luteinizing**
 hormone-releasing hormone (**LHRH**)
 AB . . . same as above), D-Ala-OH, D- or L-Glu, Sar-NH₂, D-Ser-NH₂,
 azaglycine, Gly-NH₂] are prepd. These peptides I are potent
 antagonists of **LHRH** and are useful for suppressing the

levels of sex hormones in mammals. Thus, CHO-D-2Nal-D-4-ClPhe-D-3Pal-Ser-MeTyr-D-Lys(Nic)-Leu-Lys(iso-Pr)-Pro-D-Ala-NH₂ [2Nal = 3-(naphth-2-yl)alanine; 4-ClPhe = 3-(4-chlorophenyl)alanine, . . . (4-methylbenzhydramine resin). A total of 27 I were prepd. and in vitro showed pA₂ values 8.8-11.46 in a test for **LHRH** antagonist potency, wherein the value of pA₂ is the neg. logarithm of the concn. of the particular antagonist test compd.. . . curve produced by the agonist leuprolide to two-fold higher concn. and typically pA₂ values of .gtoreq.9.5 are indicative of good **LHRH** antagonist activity, with values of .gtoreq.10.0 being preferred. MeCH₂CO-D-2Nal-D-4ClPhe-D-3Pal-Ser-MeTyr-D-Cit-Leu-Arg-Pro-D-Ala-NH₂ (Cit = citrulline) showed the highest pA₂ value (11.46).

- ST LH releasing hormone analog; decapeptide prepn **LHRH**
antagonist; sex hormone mammal suppressant
- IT Peptides, preparation
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(deca-, prepn. of N-acyldecapeptides as LH-releasing hormone (**LHRH**) antagonists)
- IT Hormones
RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)
(sex, prepn. of decapeptides as LH-releasing hormone (**LHRH**) antagonists for suppressing sex hormone in mammals)
- IT 79-14-1, reactions
RL: RCT (Reactant)
(acylation of peptide in prepn. of decapeptides as LH-releasing hormone (**LHRH**) antagonists)
- IT 64-18-6, Formic acid, reactions
RL: RCT (Reactant)
(formylation of peptide in prepn. of decapeptides as LH-releasing hormone (**LHRH**) antagonists)
- IT 338-69-2D, D-Alanine, p-methylbenzhydramine resin-bound
13139-15-6 13836-37-8 15761-39-4 23680-31-1 57292-44-1
57817-43-3 76985-10-9 98266-33-2 121080-95-3 122546-52-5
125323-99-1
RL: RCT (Reactant)
(peptide coupling in prepn. of decapeptides as LH-releasing hormone (**LHRH**) antagonists)
- IT 168158-12-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and acylation with glycolic acid in prepn. of decapeptides as LH-releasing hormone (**LHRH**) antagonist)
- IT **168157-44-6P 168157-46-8P 168157-48-0P**
168157-50-4P 168157-52-6P 168157-54-8P
168157-56-0P 168157-58-2P 168157-60-6P
168157-62-8P 168157-64-0P 168157-66-2P
168157-68-4P 168157-70-8P 168157-72-0P
168157-74-2P 168157-76-4P 168157-78-6P
168157-80-0P 168157-82-2P 168157-84-4P 168157-86-6P
168157-88-8P 168157-90-2P 168157-92-4P 168157-94-6P
168157-96-8P 168157-98-0P 168158-00-7P 168158-02-9P
168158-04-1P 168158-06-3P 168158-08-5P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological

study); PREP (Preparation); USES (Uses)
 (prepn. of decapeptides as LH-releasing hormone (**LHRH**)
 antagonists)

- IT 9034-40-6P, **Luteinizing** hormone-releasing hormone
 RL: BPN (Biosynthetic preparation); BSU (Biological study,
 unclassified); MSC (Miscellaneous); BIOL (Biological study); PREP
 (Preparation)
 (prepn. of decapeptides as LH-releasing hormone (**LHRH**)
 antagonists)
- IT **168158-09-6DP**, p-methylbenzhydrylamine resin-bound
 168158-10-9DP, p-methylbenzhydrylamine resin-bound 168158-11-0DP,
 p-methylbenzhydrylamine resin-bound
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
 (prepn., resin-cleavage, and deprotection in prepn. of
 decapeptides as LH-releasing hormone (**LHRH**)
 antagonists)

L14 ANSWER 20 OF 59 CAPLUS COPYRIGHT 1997 ACS

AN 1995:686662 CAPLUS

DN 123:65697

AU Cannon, John B.; Krill, Steven L.; Porter, William R.

TI Physicochemical Properties of **A-75998**, an
 Antagonist of **Luteinizing** Hormone Releasing Hormone

SO J. Pharm. Sci. (1995), 84(8), 953-8

CODEN: JPMSAE; ISSN: 0022-3549

AN 1995:686662 CAPLUS

DN 123:65697

AB The physicochem. properties of **A-75998**, a
 synthetic antagonist of LH releasing hormone with potential for
 treatment of hormone-sensitive cancers and endometriosis, are
 described. An accelerated soln. stability study indicated that the
 compd. is relatively stable and showed a U-shaped pH-rate profile,
 with max. stability between pH 4.5 and 6.5. The acid dissocn.
 behavior of **A-75998** was examd. by UV-visible
 spectrophotometry at 25.degree. in a series of buffers (pH 1-13).
 The data were fit to a model in which the dissocns. of all four
 ionizable groups contributed to changes in the absorbance. The
 estd. macroscopic acid dissocn. consts. were $p\beta_1 = 3.230$,
 $p\beta_2 = 4.885$, $p\beta_3 = 9.871$, and $p\beta_4 = 11.026$. The
 corresponding microscopic dissocn. consts. were $pK_1 = 3.24$
 (nicotiny), $pK_2 = 4.88$ (pyridyl), $pK_5 = 9.91$ (tyrosyl), and $pK_6 =$
 10.99 (isopropyllysyl). The apparent n-octanol/water partition
 coeffs. were measured from pH 2 to 13, and the profile was
 consistent with the expected acid-dissocn. behavior. While
 appearing fairly water-sol. at pH <5, dynamic light scattering of
A-75998 in pH 4.5 buffer indicated the formation
 of aggregates of nonuniform size distribution. **A-**
75998 exhibited reverse or thermal gelation; sodium chloride
 exacerbates this gel formation and self-assocn. Surface activity
 was pH-dependent, but no evidence was found for micelle formation.
 Based on the results, development of a parenteral formulation of
A-75998 appears feasible, provided that
 aggregation can be minimized.

TI Physicochemical Properties of **A-75998**, an
 Antagonist of **Luteinizing** Hormone Releasing Hormone

AB The physicochem. properties of **A-75998**, a
 synthetic antagonist of LH releasing hormone with potential for

treatment of hormone-sensitive cancers and endometriosis, are described. An accelerated. . . stable and showed a U-shaped pH-rate profile, with max. stability between pH 4.5 and 6.5. The acid dissocn. behavior of **A-75998** was examd. by UV-visible spectrophotometry at 25.degree. in a series of buffers (pH 1-13). The data were fit to a. . . the profile was consistent with the expected acid-dissocn. behavior. While appearing fairly water-sol. at pH <5, dynamic light scattering of **A-75998** in pH 4.5 buffer indicated the formation of aggregates of nonuniform size distribution. **A-75998** exhibited reverse or thermal gelation; sodium chloride exacerbates this gel formation and self-assocn. Surface activity was pH-dependent, but no evidence was found for micelle formation. Based on the results, development of a parenteral formulation of **A-75998** appears feasible, provided that aggregation can be minimized.

IT Decomposition

Ionization in liquids

(physicochem. properties of **A-75998** LH
releasing hormone antagonist)

IT 135215-95-1

RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(physicochem. properties of **A-75998** LH
releasing hormone antagonist)

L14 ANSWER 21 OF 59 CAPLUS COPYRIGHT 1997 ACS

AN 1995:665398 CAPLUS

DN 123:340846

AU Rivier, Jean E.; Jiang, Guangcheng; Porter, John; Hoeger, Carl; Craig, A. Grey; Corrigan, Anne; Vale, Wylie; Rivier, Catherine L.

TI **Gonadotropin**-Releasing Hormone Antagonists: Novel Members of the Azaline B Family

SO J. Med. Chem. (1995), 38(14), 2649-62

CODEN: JMCMAR; ISSN: 0022-2623

AN 1995:665398 CAPLUS

DN 123:340846

AB A series of antagonists of **gonadotropin**-releasing hormone (**GnRH**) homologous to azaline B ([Ac-DNall,DCpa2,DPal3,Aph5(Atz),DAph6(Atz),ILys8,DAla10]**GnRH**) was synthesized, characterized, and tested in a rat antiovulatory assay (AOA). Selected analogs were also tested in both an in vitro dispersed rat pituitary cell culture assay for inhibition of **GnRH**-stimulated LH release and an in vitro histamine release assay. The duration of action of some of the most potent and safest analogs in those assays was also detd. in the castrated male rat in order to measure the extent (efficacy and duration of action) of inhibition of LH release. Structurally, this series of analogs has novel substitutions (X and Y) in the structure of the azaline B precursor: [Ac-DNall,DCpa2,DPal3,Aph5(X),DAph6(Y),ILys8,DAla10]**GnRH**. These substitutions were designed to confer increased hydrophilicity as compared to that of azaline B (detd. by relative retention times on a C18 reverse phase column using a triethylammonium phosphate buffer at pH 7.3) or to make them more easily accessible synthetically. Some bulky substituents were introduced in order to probe the spatial limitations of the receptor's cavity. These substitutions include acylated

M. Borin 08/08/97

4-aminophenylalanine at positions 5 and/or 6 (29 analogs), N.alpha.-methylated backbone substitutions (six analogs), N.omega.-isopropylaminophenylalanine at position 8, and hydrophilic amino acids at position 1. Out of 20 novel analogs tested for long duration of action in this series, only seven had relative potencies and/or duration of action comparable to those of azaline B.

TI **Gonadotropin-Releasing Hormone Antagonists: Novel Members of the Azaline B Family**

AB A series of antagonists of **gonadotropin-releasing hormone (GnRH)** homologous to azaline B ([Ac-DNal1,DCpa2,DPal3,Aph5(Atz),DAph6(Atz),ILys8,DAla10]**GnRH**) was synthesized, characterized, and tested in a rat antioviulatory assay (AOA). Selected analogs were also tested in both an in vitro dispersed rat pituitary cell culture assay for inhibition of **GnRH**-stimulated LH release and an in vitro histamine release assay. The duration of action of some of the most potent and. . . release. Structurally, this series of analogs has novel substitutions (X and Y) in the structure of the azaline B precursor: [Ac-DNal1,DCpa2,DPal3,Aph5(X),DAph6(Y),ILys8,DAla10]**GnRH**. These substitutions were designed to confer increased hydrophilicity as compared to that of azaline B (detd. by relative retention times).

ST **gonadotropin releasing hormone antagonist azaline B**

IT Peptides, preparation

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation) (synthesis and activities of azaline B analogs as **gonadotropin-releasing hormone antagonists**)

IT 134457-26-4P, Azaline 134457-28-6P, Azaline B 160618-03-1P, Azaline C **161356-80-5P** 170157-08-1P 170157-09-2P 170157-10-5P 170157-11-6P 170157-12-7P 170157-13-8P, Acyline 170157-14-9P 170157-15-0P 170157-16-1P 170157-17-2P 170157-18-3P **170157-19-4P** 170157-20-7P 170157-21-8P 170157-22-9P 170157-23-0P 170157-24-1P 170157-25-2P 170157-26-3P 170157-27-4P 170157-28-5P 170157-29-6P 170157-30-9P 170157-31-0P 170157-32-1P 170157-33-2P 170157-34-3P 170157-35-4P 170157-36-5P 170157-37-6P 170157-38-7P 170157-39-8P 170157-40-1P 170157-41-2P 170157-42-3P 170157-43-4P 170157-44-5P 170157-45-6P 170157-46-7P 170157-47-8P 170157-48-9P 170421-64-4P 170421-65-5P 170421-66-6P

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation) (synthesis and activities of azaline B analogs as **gonadotropin-releasing hormone antagonists**)

IT 9034-40-6, **Gonadotropin-releasing hormone**

RL: BSU (Biological study, unclassified); BIOL (Biological study) (synthesis and activities of azaline B analogs as **gonadotropin-releasing hormone antagonists**)

IT 63-91-2, Phenylalanine, reactions 594-65-0 619-23-8 1068-90-2, Diethyl acetamidomalonate 4377-41-7 5241-64-5 7764-95-6 13139-15-6 13734-34-4 13836-37-8 15761-39-4 23680-31-1 47689-67-8 55533-24-9 57292-44-1 76985-10-9 84624-27-1 98266-33-2 115186-31-7, BOC-D-Lys(FMOC)-OH 121080-95-3, BOC-D-Cit-OH 135101-24-5 150828-96-9, BOC-Orn(FMOC)-OH 163336-15-0, BOC-D-Orn(FMOC)-OH
RL: RCT (Reactant)

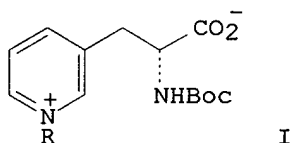
- (synthesis and activities of azaline B analogs as
gonadotropin-releasing hormone antagonists)
- IT 2566-30-5P, N.alpha.-Methyl-L-phenylalanine 5432-19-9P
 34891-76-4P 37553-65-4P 70663-55-7P 70663-56-8P 102164-99-8P
 131980-25-1P 131980-29-5P 137452-49-4P 158741-21-0P
 170157-49-0P 170157-50-3P 170157-51-4P 170157-52-5P
 170157-53-6P 170157-54-7P 170157-55-8P 170157-56-9P
 170157-59-2P 170157-60-5P 170157-62-7P 170157-66-1P
 170421-67-7P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
 (synthesis and activities of azaline B analogs as
gonadotropin-releasing hormone antagonists)
- IT 164361-76-6P 170157-57-0P 170157-58-1P 170157-61-6P
 170157-63-8P 170157-64-9P 170157-65-0P 170157-67-2P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (synthesis and activities of azaline B analogs as
gonadotropin-releasing hormone antagonists)
- L14 ANSWER 23 OF 59 CAPLUS COPYRIGHT 1997 ACS
 AN 1995:604147 CAPLUS
 DN 123:1054
 AU Gordon, K.; Danforth, D. R.; Williams, R. F.; Hodgen, G. D.
 TI Comparison of **GnRH** antagonist compounds: primate studies
 for selection of clinically useful analogs
 SO **GnRH**, **GnRH** Analogs, **Gonadotropins** **Gonadal** Pept., Proc. Organon Round
 Table Conf., 3rd (1993), Meeting Date 1992, 229-38. Editor(s):
 Bouchard, Philippe. Publisher: Parthenon Publ., London, UK.
 CODEN: 61MSAR
 AN 1995:604147 CAPLUS
 DN 123:1054
 AB A review, with 36 refs., on preclin. studies with the third
 generation **GnRH** antagonist Antide and a fourth generation
 compd. **A 75998**.
 TI Comparison of **GnRH** antagonist compounds: primate studies
 for selection of clinically useful analogs
 AB A review, with 36 refs., on preclin. studies with the third
 generation **GnRH** antagonist Antide and a fourth generation
 compd. **A 75998**.
 ST review **LHRH** antide A75998
 IT Primate
 (**GnRH** antagonist clin. evaluation with primates)
 IT 9034-40-6, **GnRH**
 RL: BAC (Biological activity or effector, except adverse); BIOL
 (Biological study)
 (**GnRH** antagonist clin. evaluation with primates)
 IT 112568-12-4, Antide **135215-95-1**, **A 75998**
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (**GnRH** antagonist clin. evaluation with primates)
- L14 ANSWER 40 OF 59 CAPLUS COPYRIGHT 1997 ACS
 AN 1993:626394 CAPLUS
 DN 119:226394
 AU Zhang, Yongliang; Tian, Zhenping; Kowalczyk, Maria; Edwards,
 Patrick; Roeske, Roger W.
 TI N-alkylation of pyridylalanine and pyridinecarboxylic acids and
 their use in synthesis of **GnRH** antagonists
 SO Tetrahedron Lett. (1993), 34(23), 3659-62

CODEN: TELEAY; ISSN: 0040-4039

AN 1993:626394 CAPLUS

DN 119:226394

GI



- AB A mild N-alkylation method has been developed for the synthesis of N-alkylated pyridiniumcarboxylic acids using Ag₂O-H₂O catalysis to enhance the low reactivity of pyridinecarboxylic acids. Two approaches were undertaken for the synthesis of a series of **GnRH** antagonists contg. pyridinium moieties at the side chain: (1) incorporation of alkylated D-pyridylalanine analogs I (Boc = Me₃CO₂C; R = Me, CH₂Ph, CHMe₂, Bu) during solid phase peptide chain assembly, and (2) coupling of the N-alkylated pyridiniumcarboxylic acid to a D-lysine .epsilon.-amino group on a solid support.
- TI N-alkylation of pyridylalanine and pyridinecarboxylic acids and their use in synthesis of **GnRH** antagonists
- AB . . . catalysis to enhance the low reactivity of pyridinecarboxylic acids. Two approaches were undertaken for the synthesis of a series of **GnRH** antagonists contg. pyridinium moieties at the side chain: (1) incorporation of alkylated D-pyridylalanine analogs I (Boc = Me₃CO₂C; R = . . .
- ST alkylation pyridinecarboxylic acid silver catalyst; pyridinecarboxylate alkylation silver oxide water; **gonadotropin** releasing hormone alkylpyridyl analog
- IT 150812-67-2P 150812-68-3P 150812-69-4P 150812-70-7P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (prepn. and solid-phase peptide coupling reactions of, in prepn. of **gonadotropin** releasing hormone analog)
- IT 59-67-6DP, Nicotinic acid, N-alkylated, side chain amides with D-lysine residues on **gonadotropin** releasing hormone analogs 98-98-6DP, Picolinic acid, N-alkylated, side chain amides with D-lysine residues on **gonadotropin** releasing hormone analogs 6938-06-3P, N-Butylnicotinate 150812-71-8P, N-Isopropylnicotinate 150812-72-9P, N-Isopropylpicolinate 150812-73-0P **150812-74-1P 150812-75-2P 150812-76-3P 150812-77-4P 150812-78-5DP**, D-lysine side chain amides with alkylated nicotinic or picolinic acids
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (prepn. of)
- IT **150828-97-0DP**, resin-bound
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (prepn., selective side chain deblocking with piperidine, and amidation of, with N-alkylated picolinic and nicotinic acid derivs.)

AN 1993:213551 CAPLUS
 DN 118:213551
 IN Deghenghi, Romano
 TI Preparation of **luteinizing** hormone releasing hormone antagonist peptides
 SO PCT Int. Appl., 20 pp.
 CODEN: PIXXD2
 PI WO 9219651 A1 921112
 PRAI US 91-690861 910425
 AN 1993:213551 CAPLUS
 DN 118:213551
 AB LH-RH antagonist peptides Ac-D-Nal-D-p-ClPhe-D-PyAla-Ser-Tyr-Lys(CONH2)-Leu-Lys(CHMe2)-Pro-R [I; R = D-Ala-NH2, NHet, Nal] = 3-(2-naphthyl)alanine, p-ClPhe = 3-(4-chlorophenyl)alanine, PyAla = 3-(3-pyridyl)alanine] and pharmaceutically acceptable salts thereof were prepd. which effectively decrease plasma levels of estrogens and androgens. Thus, I (R = D-Ala-NH2) (II) was prepd. by solid-phase methods using a benzhydrylamine resin on a polystyrene support with N.alpha.-9-fluorenylmethoxycarbonyl (Fmoc) protection. II exhibited increased levels of potency (>10 .times.) relative to Antide, while at the same time minimizing histamine releasing properties, vascular permeability (or edematogenic effects), hypotension, poor water soly., and inadequate duration of action assocd. with known LH-RH antagonists.
 TI Preparation of **luteinizing** hormone releasing hormone antagonist peptides
 ST **LHRH** antagonist peptide Merrifield synthesis
 IT **147426-19-5P 147426-20-8P 147426-21-9P**
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (prepn. of, by solid-phase methods and LH-RH antagonistic activity of)

L14 ANSWER 44 OF 59 CAPLUS COPYRIGHT 1997 ACS
 AN 1993:73773 CAPLUS
 DN 118:73773
 AU Nestor, John J., Jr.; Tahilramani, Ram; Ho, Teresa L.; Goodpasture, Jessie C.; Vickery, Brian H.; Ferrandon, Pierre
 TI Potent **gonadotropin** releasing hormone antagonists with low histamine-releasing activity
 SO J. Med. Chem. (1992), 35(21), 3942-8
 CODEN: JMCMAR; ISSN: 0022-2623
 AN 1993:73773 CAPLUS
 DN 118:73773
 AB The incorporation of Arg residues into position 6 of **gonadotropin**-releasing hormone antagonists had resulted in compds. with increased in vivo potency but also made these analogs potent mast cell degranulators. Substitution of position 8 by hArg(R)2 (NG,NG-dialkylhomoarginine) was examd, based on the hypotheses that the Arg-Pro sequence is of major importance for this histamine-releasing side effect and that shielding of the charge may be an effective way to block degranulation. Analogs in four series were evaluated: (A) [N-Ac-D-Nal(2), 1D-pCl-Phe2,D-Pal(3)3,6,Arg5,hArg(R)28,D-Ala10]**GnRH**, (B) [N-Ac-D-Nal(2)1,D-pCl-Phe2,D-Pal(3)3,6,hArg(R)25,8,D-Ala10]**GnRH**, (C) [N-Ac-D-Nal(2)1,D-pCl-Phe2,D-Pal(3)3,6,hArg(R)28,D-Ala10]**GnRH**, (D) [N-Ac-D-Nal(2)1,D-pCl-Phe2,D-Pal(3)3,D-hArg(R)26,hArg(R)28,D-Ala10]**GnRH**. Although substitution R
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= Et2, Bu4, (CH2)3, and (CH2CF3)2 was tested, in each series substitution with hArg(Et)2 gave the best results. Two compds. were considered for clin. evaluation: [N-Ac-D-Nal(2)1,D-pCl-Phe2,D-Pal(3)3,6,hArg(Et)28,D-Ala10]**GnRH** and [N-Ac-D-Nal(2)1,D-pCl-Phe2,D-Pal(3)3, D-hArg(Et)26,hArg(Et)28,D-Ala10]**GnRH** (ganirelix acetate). These compds. had high potency for ovulation suppression and low histamine-releasing potency in vitro (ED50 = 0.6-0.29 .mu.g/rat and EC50 = 196-13 .mu.g/mL, resp). Ganirelix is currently in Phase II clin. trails and appears to be the most potent **GnRH** antagonist tested in humans (based upon ED50 for 24-h suppression of testosterone levels).

- TI Potent **gonadotropin** releasing hormone antagonists with low histamine-releasing activity
- AB The incorporation of Arg residues into position 6 of **gonadotropin**-releasing hormone antagonists had resulted in compds. with increased in vivo potency but also made these analogs potent mast cell degranulators.. . . shielding of the charge may be an effective way to block degranulation. Analogs in four series were evaluated: (A) [N-Ac-D-Nal(2), 1D-pCl-Phe2,D-Pal(3)3,6,Arg5,hArg(R)28,D-Ala10]**GnRH**, (B) [N-Ac-D-Nal(2)1,D-pCl-Phe2,D-Pal(3)3,6,hArg(R)25,8,D-Ala10]**GnRH**, (C) [N-Ac-D-Nal(2)1,D-pCl-Phe2,D-Pal(3)3,6,hArg(R)28,D-Ala10]**GnRH**, (D) [N-Ac-D-Nal(2)1,D-pCl-Phe2,D-Pal(3)3,D-hArg(R)26,hArg(R)28,D-Ala10]**GnRH**. Although substitution R = Et2, Bu4, (CH2)3, and (CH2CF3)2 was tested, in each series substitution with hArg(Et)2 gave the best results. Two compds. were considered for clin. evaluation: [N-Ac-D-Nal(2)1,D-pCl-Phe2,D-Pal(3)3,6,hArg(Et)28,D-Ala10]**GnRH** and [N-Ac-D-Nal(2)1,D-pCl-Phe2,D-Pal(3)3, D-hArg(Et)26,hArg(Et)28,D-Ala10]**GnRH** (ganirelix acetate). These compds. had high potency for ovulation suppression and low histamine-releasing potency in vitro (ED50 = 0.6-0.29 .mu.g/rat. . . EC50 = 196-13 .mu.g/mL, resp). Ganirelix is currently in Phase II clin. trails and appears to be the most potent **GnRH** antagonist tested in humans (based upon ED50 for 24-h suppression of testosterone levels).
- ST **LHRH** antagonist structure activity; ovulation inhibition **gonadotropin** releasing hormone antagonist; contraceptive **gonadotropin** releasing hormone antagonist prepn; histamine **gonadotropin** releasing hormone antagonist structure; ganirelix ovulation inhibition histamine release structure
- IT Mast cell
(degranulation of, **gonadotropin**-releasing hormone antagonists effect on)
- IT Ovulation
(inhibitors, **gonadotropin**-releasing hormone antagonists as, prepn. and histamine-releasing activity of, structure in relation to)
- IT Molecular structure-biological activity relationship
(**gonadotropin** release-inhibiting, of peptide **gonadotropin**-releasing hormone antagonist)
- IT Molecular structure-biological activity relationship
(histamine-releasing, of peptide **gonadotropin**-releasing hormone antagonist)
- IT 86855-16-5 89662-30-6 124904-93-4 124926-38-1 125378-68-9
133951-43-6 **133951-44-7** 133972-58-4 144271-50-1
144271-51-2 144271-52-3 144271-54-5 144271-55-6 144271-56-7
144271-57-8 144271-58-9 144271-59-0 144271-60-3 144271-61-4

144271-62-5 144271-63-6 144271-64-7 **144271-65-8**
 144271-66-9 144271-67-0 144302-83-0 144302-84-1 144302-85-2
 144302-86-3 144302-87-4

RL: BIOL (Biological study)

(**gonadotropin**-releasing hormone antagonist and histamine-releasing activities of)

IT 51-45-6, Histamine, biological studies

RL: BIOL (Biological study)

(release of, **gonadotropin**-releasing hormone antagonist effect on)

L14 ANSWER 47 OF 59 CAPLUS COPYRIGHT 1997 ACS

AN 1991:632885 CAPLUS

DN 115:232885

IN Haviv, Fortuna; Greer, Jonathan

TI Preparation of **LHRH** analogs

SO Eur. Pat. Appl., 79 pp.

CODEN: EPXXDW

PI EP 413209 A1 910220

PRAI US 89-390572 890807

US 90-548512 900710

AN 1991:632885 CAPLUS

DN 115:232885

AB **LHRH** analogs A-B-C-D-E-F-G-H-I-J [A = amino acyl, e.g., L- or D-pyroglutamyl, N-acetyl-L-prolyl, etc.; B = bond, amino acid residue, e.g., L- or D-Trp, etc.; C = amino acid residue, e.g., L- or D-Trp, D-Pro, etc.; D = amino acid residue, e.g., Pro, Pro(4-OH), etc.; E = amino acid residue, e.g., L-Tyr, L-Tyr(Me), etc.; F = amino acid residue; G = amino acid residue, e.g., L-Leu, L-Ile, etc., or F and G taken together are substituted .gamma.-lactam residue; H = NR1CH[(CH2)pR2]CO; R1 = H, Me, Et, Pr, Me2CH; R2 = (alkyl)amino(cyclohexyl), etc.; p = 1-4; I = imino acid or aliph. amino acid residue, e.g., L-Pro, L-MeAla, etc.; J = 1-pyrrolidinyl, 1-piperidinyl, 4-morpholinyl, or amino acid residue, e.g., D-alanylamine, etc.; with provisos] were prepd. Thus, H-(pyro)Glu-His-Trp-MeSer-Tyr-D-Leu-Leu-Arg-Pro-NH₂ (I) was prepd. using solid phase methods by sequential coupling of appropriate protected amino acids followed by deprotection and isolation as the trifluoroacetate salt. I.cntdot.CF₃CO₂H had an ED₅₀ of 7.20 .mu.g/kg i.v. for LH release in castrated rats, compared to 100 .mu.g/kg for **LHRH**.

TI Preparation of **LHRH** analogs

AB **LHRH** analogs A-B-C-D-E-F-G-H-I-J [A = amino acyl, e.g., L- or D-pyroglutamyl, N-acetyl-L-prolyl, etc.; B = bond, amino acid residue, e.g., L- . . . salt. I.cntdot.CF₃CO₂H had an ED₅₀ of 7.20 .mu.g/kg i.v. for LH release in castrated rats, compared to 100 .mu.g/kg for **LHRH**.

ST **LHRH** analog; agonist **LHRH**; antagonist **LHRH**

IT 78981-25-6DP, benzhydrylamine resin-bound 94849-39-5DP, 4-methylbenzhydrylamine resin 135216-06-7DP, 4-methylbenzhydrylamine resin bound **135216-07-8DP**, resin bound

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation) (prepn. and peptide coupling of, in prepn. of LH-RH agonists)

IT 125323-81-1P 125323-86-6P 125323-88-8P 125323-90-2P
 125323-91-3P 125323-92-4P 125323-93-5P 125323-94-6P

M. Borin 08/08/97

us Pat 5110904

N

125323-96-8P 125323-97-9P 125324-12-1P 135185-09-0P
 135185-11-4P 135185-12-5P 135185-13-6P 135185-14-7P
 135185-15-8P 135185-16-9P 135185-17-0P 135185-19-2P
 135185-21-6P 135185-23-8P 135185-25-0P 135185-27-2P
 135185-29-4P 135185-31-8P 135185-33-0P 135185-35-2P
 135185-37-4P 135185-39-6P 135185-41-0P 135185-43-2P
 135185-45-4P 135185-47-6P 135185-49-8P 135185-50-1P
 135185-51-2P 135185-53-4P 135185-55-6P **135185-57-8P**
 135185-59-0P 135185-61-4P 135185-63-6P **135185-65-8P**
135185-67-0P 135185-69-2P 135185-70-5P
 135185-71-6P 135185-72-7P 135185-73-8P 135185-74-9P
 135185-75-0P 135185-76-1P 135185-77-2P 135185-78-3P
135215-96-2P 135215-97-3P 135215-99-5P 135216-01-2P
 135216-02-3P 135216-03-4P **135245-25-9P**

RL: SPN (Synthetic preparation); PREP (Preparation)
 (prepn. of, as LH-RH agonist)

IT 9034-40-6DP, LH-RH, analogs **135185-66-9DP**,
 benzylhydramine resin-bound
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (prepn. of, as LH-RH agonists)

L14 ANSWER 48 OF 59 CAPLUS COPYRIGHT 1997 ACS

AN 1991:492888 CAPLUS

DN 115:92888

AU Theobald, Paula; Porter, John; Rivier, Catherine; Corrigan, Anne;
 Perrin, Marilyn; Vale, Wylie; Rivier, Jean; Hook, William;
 Siraganian, Reuben

TI Novel **gonadotropin**-releasing hormone antagonists:
 peptides incorporating modified N.omega.-cyanoguanidino moieties
 SO J. Med. Chem. (1991), 34(8), 2395-402
 CODEN: JMCMAR; ISSN: 0022-2623

AN 1991:492888 CAPLUS

DN 115:92888

AB In order to minimize the deleterious effects of histamine release
 resulting from the administration of some potent
gonadotropin-releasing hormone (**GnRH**) antagonists
 to rats and humans, various arginine residues were replaced with the
 less basic N.omega.-cyano-N.omega.'-alkyl- or -arylhomarginine,
 -arginine, or -p-aminophenylalanine and N.omega.-triazolyllysine,
 -ornithine, or -p-aminophenylalanine residues in active analogs.
 These novel analogs were synthesized on a solid-phase support via a
 two-step modification of the N.omega.-NH₂ of lysine, ornithine, or
 p-aminophenylalanine residues in otherwise protected resin bound
 peptides. Most analogs were tested in the rat antioviulatory assay
 (AOA) and three in vitro assays: a pituitary cell culture assay, a
 binding assay to pituitary cell membranes, and a histamine release
 assay. Introduction of the cyanoguanidino and N.omega.-triazolyl
 moieties into **GnRH** analogs yielded several water-sol.
 antagonists which showed a desirable therapeutic ratio (low
 histamine release activity to high in vivo potency). Among them,
 Azaline [[Ac-D-Nal1,D-Cpa2,D-Pal3,Lys5(atz),D-
 Lys6(atz),Lys(CHMe2)8,D-Ala10]**GnRH** [Nal =
 3-(2-naphthyl)alanine, Cpa = 4-chlorophenylalanine, Pal =
 3-(3-pyridyl)alanine, atz = 3-amino-1H-1,2,4-triazol-5-yl]]
 inhibited ovulation in the rat by 90% at 2 .mu.g/rat with an ED₅₀ in
 the in vitro histamine release assay, comparable to that of
GnRH itself.

TI Novel **gonadotropin**-releasing hormone antagonists:
 peptides incorporating modified N.omega.-cyanoguanidino moieties

AB In order to minimize the deleterious effects of histamine release
 resulting from the administration of some potent
gonadotropin-releasing hormone (**GnRH**) antagonists
 to rats and humans, various arginine residues were replaced with the
 less basic N.omega.-cyano-N.omega.'-alkyl- or -arylhomoarginine,
 -arginine, or -p-aminophenylalanine. . . a binding assay to
 pituitary cell membranes, and a histamine release assay.
 Introduction of the cyanoguanidino and N.omega.-triazolyl moieties
 into **GnRH** analogs yielded several water-sol. antagonists
 which showed a desirable therapeutic ratio (low histamine release
 activity to high in vivo potency). Among them, Azaline
 [[Ac-D-Nal1,D-Cpa2,D-Pal3,Lys5(atz),D-Lys6(atz),Lys(CHMe2)8,D-Ala10]
GnRH [Nal = 3-(2-naphthyl)alanine, Cpa =
 4-chlorophenylalanine, Pal = 3-(3-pyridyl)alanine, atz =
 3-amino-1H-1,2,4-triazol-5-yl]] inhibited ovulation in the rat by
 90% at 2 .mu.g/rat with an ED50 in the in vitro histamine release
 assay, comparable to that of **GnRH** itself.

ST **gonadotropin** releasing hormone cyanoguanidine analog;
 histamine release cyanoguanidino **gonadotropin**;
 antiovolutary cyanoguanidino **gonadotropin**; ovulation
 inhibitor cyanoguanidino **gonadotropin**; Azaline prepn
 ovulation inhibitor

IT Ovulation
 (inhibition of, by **gonadotropin**-releasing hormone
 cyanoguanidine analogs)

IT 33515-09-2, **Gonadotropin**-releasing hormone
 RL: RCT (Reactant)
 (antagonists for, cyanoguanidino analogs as)

IT 130883-26-0P 134457-18-4P 134457-20-8P 134457-21-9P
 134457-23-1P 134457-24-2P 134457-25-3P 134457-29-7P
 134457-30-0P 134457-31-1P 134457-38-8P 134457-40-2P
 134457-43-5P 134457-44-6P 134457-46-8P 134457-47-9P
 134457-48-0P 134457-49-1P 134457-50-4P **134457-56-0P**
134457-57-1P 134457-62-8P 134485-03-3P 134485-04-4P
 134485-05-5P 134485-07-7P 134485-08-8P 134485-13-5P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (prepn. and antiovolutary activity of)

IT 134457-19-5P 134457-26-4P 134457-27-5P 134457-28-6P
 134457-32-2P 134457-33-3P 134457-34-4P **134457-35-5P**
 134457-36-6P 134457-37-7P 134457-39-9P 134457-41-3P
 134457-42-4P 134457-45-7P 134457-51-5P 134457-52-6P
134457-53-7P 134457-54-8P 134457-55-9P 134457-58-2P
 134457-59-3P 134457-61-7P 134457-63-9P 134485-09-9P
 134485-10-2P 134485-11-3P 134485-12-4P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (prepn. and antiovolutary and histamine releasing activities of)

IT 74-89-5P, Methylamine, reactions 75-31-0P, Isopropylamine,
 reactions 108-91-8P, Cyclohexylamine, reactions 109-73-9P,
 Butylamine, reactions 109-79-5P, Butanethiol 111-26-2P,
 Hexylamine 3731-51-9P, 2-(Aminomethyl)pyridine 79463-77-7P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (prepn. and condensation of, with amino side chains in
gonadotropin releasing hormone analogs)

IT 114346-31-5P
 RL: SPN (Synthetic preparation); PREP (Preparation)

08/480494 APS,STN

(prepn. and solid-phase peptide coupling reactions of,
gonadotropin releasing hormone antagonists from)
IT 51-45-6, Histamine, biological studies
RL: BIOL (Biological study)
(release of, by **gonadotropin**-releasing hormone
cyanoguanidine analogs)

L14 ANSWER 50 OF 59 CAPLUS COPYRIGHT 1997 ACS
AN 1991:240782 CAPLUS
DN 114:240782
AU Nestor, J. J., Jr.; Tahilramani, R.; Ho, T. L.; Goodpasture, J. C.;
Vickery, B. H.; Ferrandon, P.
TI Design of **luteinizing** hormone releasing hormone
antagonists with reduced potential for side effects
SO Pept., Proc. Eur. Pept. Symp., 20th (1989), Meeting Date 1988,
592-4. Editor(s): Jung, Guenther; Bayer, Ernst. Publisher: de
Gruyter, Berlin, Fed. Rep. Ger.
CODEN: 57ACAI
AN 1991:240782 CAPLUS
DN 114:240782
AB A report from a symposium on the antiovolatory and mast cell
degranulating activities of D-Ng,Ng'-dialkylhomoarginine derivs. of
LH-RH antagonists. Detirelix analogs Ac-D-Nal-D-Phe(p-Cl)-D-Pal-Ser-
Tyr-X-Leu-hArg(Et)2-Pro-D-Ala-NH2 [I; Nal = 3-(2-naphthyl)alanine,
Pal = 3-(3-pyridyl)alanine, hArg(Et)2 = Ng,Ng'-diethylhomoarginine;
X = D-Pal, D-hArg(Et)2] had 6-8-fold improved antagonistic potency
compared to detirelix, and a 70-1000-fold decrease in toxicity. I
[X = D-hArg(Et)2] was selected for clin. trials.
TI Design of **luteinizing** hormone releasing hormone
antagonists with reduced potential for side effects
IT 89662-30-6D, Detirelix, dialkylhomoarginine analogs 120128-39-4
120128-56-5 124904-93-4 124926-38-1 133951-43-6
133951-44-7 133951-45-8 133972-58-4
RL: BIOL (Biological study)
(antiovolatory and mast cell degranulation activities of)

=> save 11-114 s480494/1

L# LIST 'L1-L14' HAS BEEN SAVED AS 'S480494/L'

=> log h

COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	94.47	1377.06
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	-14.49	-14.95

SESSION WILL BE HELD FOR 60 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 10:25:23 ON 08 AUG 1997

M. Borin 08/08/97

FILE 'REGISTRY' ENTERED AT 12:33:06 ON 22 AUG 1997
L1 22 S AFASYNLKPA/SQEF

=> d his

(FILE 'HOME' ENTERED AT 12:32:55 ON 22 AUG 1997)

FILE 'REGISTRY' ENTERED AT 12:33:06 ON 22 AUG 1997
L1 22 S AFASYNLKPA/SQEF
L2 11 S L1 AND GLN-6/NTE
L3 11 S L1 NOT L2
L4 0 S US 95-480494/PRAI

FILE 'CAPLUS' ENTERED AT 12:44:14 ON 22 AUG 1997

FILE 'REGISTRY' ENTERED AT 12:44:29 ON 22 AUG 1997
SET SMARTSELECT ON
L5 SEL L1 1- CHEM : 25 TERMS
SET SMARTSELECT OFF

FILE 'CAPLUS' ENTERED AT 12:44:32 ON 22 AUG 1997
L6 5 S L5
L7 0 S US 95-480494/PRAI
L8 0 S US 95-480494
L9 0 S 480494
L10 0 S 480494/BIB

FILE 'REGISTRY' ENTERED AT 12:48:15 ON 22 AUG 1997

<-----User Break----->

=> all sequences with Gln-12 set (but these are modified Gln)

'ALL' IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> d 12 sqd,bib

L2 ANSWER 1 OF 11 REGISTRY COPYRIGHT 1997 ACS
RN 186836-56-6 REGISTRY
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL 10
NTE modified

type	location		description
terminal mod.	Ala-1	-	N-acetyl
terminal mod.	Ala-10	-	C-terminal amide
modification	-	-	undetermined modification
modification	Ala-1	-	2-naphthalenyl<2-Naph>
modification	Phe-2	-	chloro<Cl>
modification	Ala-3	-	3-pyridinyl<3Py>

pas-nb/sqefp.
on bly
Thw
Don.

modified
bly.

modification Gln-6 - 1-methylethyl<i-Pr>
modification Lys-8 - 1-methylethyl<i-Pr>

SEQ 1 AFASYQLKPA

=====

HITS AT: 1-10

AN 126:152828 CA

TI LHRH antagonist synthetic peptide analogs for use as cancer
inhibitors, contraceptives, or other pharmaceuticals

IN Roeske, Roger W.

PA Indiana University Foundation, USA; Roeske, Roger W.

SO PCT Int. Appl., 52 pp.
CODEN: PIXXD2

PI WO 9640757 A2 961219

DS W: AU, CA, JP, US
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT,
SE

AI WO 96-US9852 960607

PRAI US 95-480494 950607

DT Patent

LA English

this case

REFERENCE 1

AN 126:152828 CA

TI LHRH antagonist synthetic peptide analogs for use as cancer
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SE

AI WO 96-US9852 960607

PRAI US 95-480494 950607

DT Patent

LA English

=> d 12 sqd,bib 2-11

L2 ANSWER 2 OF 11 REGISTRY COPYRIGHT 1997 ACS

RN 186836-55-5 REGISTRY

FS 3D CONCORD; PROTEIN SEQUENCE; STEREOSEARCH

SQL 10

NTE modified

type	location		description
terminal mod.	Ala-1	-	N-acetyl
terminal mod.	Ala-10	-	C-terminal amide
modification	Ala-1	-	2-naphthalenyl<2-Naph>
modification	Phe-2	-	chloro<Cl>
modification	Ala-3	-	3-pyridinyl<3Py>
modification	Gln-6	-	1-methylethyl<i-Pr>
modification	Lys-8	-	1-methylethyl<i-Pr>

SEQ 1 AFASYQLKPA

HITS AT: 1-10

M. Borin 08/21/97

L2 ANSWER 3 OF 11 REGISTRY COPYRIGHT 1997 ACS
 RN 186836-54-4 REGISTRY
 FS PROTEIN SEQUENCE; STEREOSEARCH
 SQL 10
 NTE modified

type	location	description
terminal mod.	Ala-1	N-acetyl
terminal mod.	Ala-10	C-terminal amide
modification	-	undetermined modification
modification	Ala-1	2-naphthalenyl<2-Naph>
modification	Phe-2	chloro<Cl>
modification	Ala-3	3-pyridinyl<3Py>
modification	Gln-6	undetermined modification
modification	Lys-8	1-methylethyl<i-Pr>

SEQ 1 AFASYQLKPA

HITS AT: 1-10

AN 126:152828 CA

TI LHRH antagonist synthetic peptide analogs for use as cancer inhibitors, contraceptives, or other pharmaceuticals

IN Roeske, Roger W.

PA Indiana University Foundation, USA; Roeske, Roger W.

SO PCT Int. Appl., 52 pp.

CODEN: PIXXD2

PI WO 9640757 A2 961219

DS W: AU, CA, JP, US

RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

AI WO 96-US9852 960607

PRAI US 95-480494 950607

DT Patent

LA English

REFERENCE 1

AN 126:152828 CA

TI LHRH antagonist synthetic peptide analogs for use as cancer inhibitors, contraceptives, or other pharmaceuticals

IN Roeske, Roger W.

PA Indiana University Foundation, USA; Roeske, Roger W.

SO PCT Int. Appl., 52 pp.

CODEN: PIXXD2

PI WO 9640757 A2 961219

DS W: AU, CA, JP, US

RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

AI WO 96-US9852 960607

PRAI US 95-480494 950607

DT Patent

LA English

L2 ANSWER 4 OF 11 REGISTRY COPYRIGHT 1997 ACS

RN 186836-53-3 REGISTRY

FS 3D CONCORD; PROTEIN SEQUENCE; STEREOSEARCH

SQL 10

NTE modified

type	location	description
------	----------	-------------

terminal mod.	Ala-1	-	N-acetyl
terminal mod.	Ala-10	-	C-terminal amide
modification	Ala-1	-	2-naphthalenyl<2-Naph>
modification	Phe-2	-	chloro<Cl>
modification	Ala-3	-	3-pyridinyl<3Py>
modification	Gln-6	-	undetermined modification
modification	Lys-8	-	1-methylethyl<i-Pr>

SEQ 1 AFASYQLKPA

HITS AT: 1-10

L2 ANSWER 5 OF 11 REGISTRY COPYRIGHT 1997 ACS
 RN 186836-37-3 REGISTRY
 FS PROTEIN SEQUENCE; STEREOSEARCH
 SQL 10
 NTE modified

type	location		description
terminal mod.	Ala-1	-	N-acetyl
terminal mod.	Ala-10	-	C-terminal amide
modification	-	-	undetermined modification
modification	Ala-1	-	2-naphthalenyl<2-Naph>
modification	Phe-2	-	chloro<Cl>
modification	Ala-3	-	3-pyridinyl<3Py>
modification	Gln-6	-	ethyl<2; Et>
modification	Lys-8	-	1-methylethyl<i-Pr>

SEQ 1 AFASYQLKPA

HITS AT: 1-10

AN 126:152828 CA
 TI LHRH antagonist synthetic peptide analogs for use as cancer inhibitors, contraceptives, or other pharmaceuticals
 IN Roeske, Roger W.
 PA Indiana University Foundation, USA; Roeske, Roger W.
 SO PCT Int. Appl., 52 pp.
 CODEN: PIXXD2
 PI WO 9640757 A2 961219
 DS W: AU, CA, JP, US
 RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
 AI WO 96-US9852 960607
 PRAI US 95-480494 950607
 DT Patent
 LA English

REFERENCE 1

AN 126:152828 CA
 TI LHRH antagonist synthetic peptide analogs for use as cancer inhibitors, contraceptives, or other pharmaceuticals
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 AI WO 96-US9852 960607

M. Borin 08/21/97

PRAI US 95-480494 950607
DT Patent
LA English

L2 ANSWER 6 OF 11 REGISTRY COPYRIGHT 1997 ACS
RN 186836-36-2 REGISTRY
FS 3D CONCORD; PROTEIN SEQUENCE; STEREOSEARCH
SQL 10
NTE modified

type	location		description
terminal mod.	Ala-1	-	N-acetyl
terminal mod.	Ala-10	-	C-terminal amide
modification	Ala-1	-	2-naphthalenyl<2-Naph>
modification	Phe-2	-	chloro<Cl>
modification	Ala-3	-	3-pyridinyl<3Py>
modification	Gln-6	-	ethyl<2; Et>
modification	Lys-8	-	1-methylethyl<i-Pr>

SEQ 1 AFASYQLKPA

HITS AT: 1-10

L2 ANSWER 7 OF 11 REGISTRY COPYRIGHT 1997 ACS
RN 186836-35-1 REGISTRY
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL 10
NTE modified

type	location		description
terminal mod.	Ala-1	-	N-acetyl
terminal mod.	Ala-10	-	C-terminal amide
modification	-	-	undetermined modification
modification	Ala-1	-	2-naphthalenyl<2-Naph>
modification	Phe-2	-	chloro<Cl>
modification	Ala-3	-	3-pyridinyl<3Py>
modification	Gln-6	-	undetermined modification
modification	Lys-8	-	1-methylethyl<i-Pr>

SEQ 1 AFASYQLKPA

HITS AT: 1-10

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SO PCT Int. Appl., 52 pp.

CODEN: PIXXD2

PI WO 9640757 A2 961219

DS W: AU, CA, JP, US

RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

AI WO 96-US9852 960607

PRAI US 95-480494 950607

DT Patent

LA English

REFERENCE 1

M. Borin 08/21/97

AN 126:152828 CA
 TI LHRH antagonist synthetic peptide analogs for use as cancer
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 IN Roeske, Roger W.
 PA Indiana University Foundation, USA; Roeske, Roger W.
 SO PCT Int. Appl., 52 pp.
 CODEN: PIXXD2
 PI WO 9640757 A2 961219
 DS W: AU, CA, JP, US
 RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT,
 SE
 AI WO 96-US9852 960607
 PRAI US 95-480494 950607
 DT Patent
 LA English

L2 ANSWER 8 OF 11 REGISTRY COPYRIGHT 1997 ACS
 RN 186836-34-0 REGISTRY
 FS 3D CONCORD; PROTEIN SEQUENCE; STEREOSEARCH
 SQL 10
 NTE modified

type	location	description
terminal mod.	Ala-1	N-acetyl
terminal mod.	Ala-10	C-terminal amide
modification	Ala-1	2-naphthalenyl<2-Naph>
modification	Phe-2	chloro<Cl>
modification	Ala-3	3-pyridinyl<3Py>
modification	Gln-6	undetermined modification
modification	Lys-8	1-methylethyl<i-Pr>

SEQ 1 AFASYQLKPA
 =====

HITS AT: 1-10

L2 ANSWER 9 OF 11 REGISTRY COPYRIGHT 1997 ACS
 RN 186835-75-6 REGISTRY
 FS PROTEIN SEQUENCE; STEREOSEARCH
 SQL 10
 NTE modified

type	location	description
terminal mod.	Ala-1	N-acetyl
terminal mod.	Ala-10	C-terminal amide
modification	-	undetermined modification
modification	Ala-1	2-naphthalenyl<2-Naph>
modification	Phe-2	chloro<Cl>
modification	Ala-3	3-pyridinyl<3Py>
modification	Gln-6	undetermined modification
modification	Lys-8	1-methylethyl<i-Pr>

SEQ 1 AFASYQLKPA
 =====

HITS AT: 1-10

AN 126:152828 CA
 TI LHRH antagonist synthetic peptide analogs for use as cancer
 inhibitors, contraceptives, or other pharmaceuticals
 IN Roeske, Roger W.
 PA Indiana University Foundation, USA; Roeske, Roger W.
 SO PCT Int. Appl., 52 pp.

CODEN: PIXXD2
 PI WO 9640757 A2 961219
 DS W: AU, CA, JP, US
 RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
 AI WO 96-US9852 960607
 PRAI US 95-480494 950607
 DT Patent
 LA English

REFERENCE 1

AN 126:152828 CA
 TI LHRH antagonist synthetic peptide analogs for use as cancer inhibitors, contraceptives, or other pharmaceuticals
 IN Roeske, Roger W.
 PA Indiana University Foundation, USA; Roeske, Roger W.
 SO PCT Int. Appl., 52 pp.
 CODEN: PIXXD2
 PI WO 9640757 A2 961219
 DS W: AU, CA, JP, US
 RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
 AI WO 96-US9852 960607
 PRAI US 95-480494 950607
 DT Patent
 LA English

L2 ANSWER 10 OF 11 REGISTRY COPYRIGHT 1997 ACS
 RN 186835-74-5 REGISTRY
 FS 3D CONCORD; PROTEIN SEQUENCE; STEREOSEARCH
 SQL 10
 NTE modified

type	location	description
terminal mod.	Ala-1	N-acetyl
terminal mod.	Ala-10	C-terminal amide
modification	Ala-1	2-naphthalenyl<2-Naph>
modification	Phe-2	chloro<Cl>
modification	Ala-3	3-pyridinyl<3Py>
modification	Gln-6	undetermined modification
modification	Lys-8	1-methylethyl<i-Pr>

SEQ 1 AFASYQLKPA

HITS AT: 1-10

L2 ANSWER 11 OF 11 REGISTRY COPYRIGHT 1997 ACS
 RN 184679-81-0 REGISTRY
 FS PROTEIN SEQUENCE; STEREOSEARCH
 SQL 10
 NTE modified

type	location	description
terminal mod.	Ala-1	N-acetyl
terminal mod.	Ala-10	C-terminal amide
modification	Ala-1	2-naphthalenyl<2-Naph>
modification	Ala-3	3-pyridinyl<3Py>
modification	Gln-6	undetermined modification
modification	Lys-8	1-methylethyl<i-Pr>

SEQ 1 AFASYQLKPA

HITS AT: 1-10

REFERENCE 1

AN 126:26943 CA
TI Structure-activity studies of GnRH antagonists having dipolar residues
AU Guo, L.; Tian, Z.; Edwards, P. J.; Zhang, Y. L.; Shobana, N.; Roeske, R. W.
CS School Medicine, Indiana University, Indianapolis, IN, 46202, USA
SO Pept.: Chem. Struct. Biol., Proc. Am. Pept. Symp., 14th (1996), Meeting Date 1995, 665-666. Editor(s): Kaumaya, Pravin T. P.; Hodges, Robert S. Publisher: Mayflower Scientific, Kingswinford, UK. CODEN: 63NTAF
DT Conference
LA English

=> d his

(FILE 'HOME' ENTERED AT 12:32:55 ON 22 AUG 1997)

FILE 'REGISTRY' ENTERED AT 12:33:06 ON 22 AUG 1997

L1 22 S AFASYNLKPA/SQFFP
L2 11 S L1 AND GLN-6/NTE
L3 11 S L1 NOT L2
L4 0 S US 95-480494/PRAI

FILE 'CAPLUS' ENTERED AT 12:44:14 ON 22 AUG 1997

FILE 'REGISTRY' ENTERED AT 12:44:29 ON 22 AUG 1997

SET SMARTSELECT ON
L5 SEL L1 1- CHEM : 25 TERMS
SET SMARTSELECT OFF

FILE 'CAPLUS' ENTERED AT 12:44:32 ON 22 AUG 1997

L6 5 S L5
L7 0 S US 95-480494/PRAI
L8 0 S US 95-480494
L9 0 S 480494
L10 0 S 480494/BIB

FILE 'REGISTRY' ENTERED AT 12:48:15 ON 22 AUG 1997

<-----User Break----->

=> all sequences with ~~ASN~~ *search everything except the modified*

'ALL' IS NOT A RECOGNIZED COMMAND

The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> s l1 and Asn-6/nte

3391 "ASN"/NTE
44145 "6"/NTE
178 ASN-6/NTE
("ASN"(W)"6")/NTE
L11 0 L1 AND ASN-6/NTE

M. Borin

08/21/97

=> d 13 sqd,bib 1-11

L3 ANSWER 1 OF 11 REGISTRY COPYRIGHT 1997 ACS
RN 186837-47-8 REGISTRY
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL 10
NTE modified

type	location	description
terminal mod.	Ala-1	N-acetyl
terminal mod.	Ala-10	C-terminal amide
modification	-	undetermined modification
modification	Ala-1	2-naphthalenyl<2-Naph>
modification	Phe-2	chloro<Cl>
modification	Ala-3	3-pyridinyl<3Py>
modification	Tyr-5	methyl<Me>
modification	Lys-8	1-methylethyl<i-Pr>

SEQ 1 AFASYNLKPA

=====

HITS AT: 1-10
AN 126:152828 CA
TI LHRH antagonist synthetic peptide analogs for use as cancer
inhibitors, contraceptives, or other pharmaceuticals
IN Roeske, Roger W.
PA Indiana University Foundation, USA; Roeske, Roger W.
SO PCT Int. Appl., 52 pp.
CODEN: PIXXD2
PI WO 9640757 A2 961219
DS W: AU, CA, JP, US
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT,
SE
AI WO 96-US9852 960607
PRAI US 95-480494 950607
DT Patent
LA English

REFERENCE 1

AN 126:152828 CA
TI LHRH antagonist synthetic peptide analogs for use as cancer
inhibitors, contraceptives, or other pharmaceuticals
IN Roeske, Roger W.
PA Indiana University Foundation, USA; Roeske, Roger W.
SO PCT Int. Appl., 52 pp.
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PI WO 9640757 A2 961219
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SE
AI WO 96-US9852 960607
PRAI US 95-480494 950607
DT Patent
LA English

L3 ANSWER 2 OF 11 REGISTRY COPYRIGHT 1997 ACS
RN 186836-46-4 REGISTRY
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL 10
NTE modified

M. Borin 08/21/97

type	location		description
terminal mod.	Ala-1	-	N-acetyl
terminal mod.	Ala-10	-	C-terminal amide
modification	-	-	undetermined modification
modification	Ala-1	-	2-naphthalenyl<2-Naph>
modification	Phe-2	-	chloro<Cl>
modification	Ala-3	-	3-pyridinyl<3Py>
modification	Lys-8	-	1-methylethyl<i-Pr>

SEQ 1 AFASYELKPA

=====

HITS AT: 1-10

AN 126:152828 CA

TI LHRH antagonist synthetic peptide analogs for use as cancer inhibitors, contraceptives, or other pharmaceuticals

IN Roeske, Roger W.

PA Indiana University Foundation, USA; Roeske, Roger W.

SO PCT Int. Appl., 52 pp.

CODEN: PIXXD2

PI WO 9640757 A2 961219

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AI WO 96-US9852 960607

PRAI US 95-480494 950607

DT Patent

LA English

REFERENCE 1

AN 126:152828 CA

TI LHRH antagonist synthetic peptide analogs for use as cancer inhibitors, contraceptives, or other pharmaceuticals

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PA Indiana University Foundation, USA; Roeske, Roger W.

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CODEN: PIXXD2

PI WO 9640757 A2 961219

DS W: AU, CA, JP, US

RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

AI WO 96-US9852 960607

PRAI US 95-480494 950607

DT Patent

LA English

L3 ANSWER 3 OF 11 REGISTRY COPYRIGHT 1997 ACS

RN 186836-24-8 REGISTRY

FS PROTEIN SEQUENCE; STEREOSEARCH

SQL 10

NTE modified

type	location		description
terminal mod.	Ala-1	-	N-acetyl
terminal mod.	Ala-10	-	C-terminal amide
modification	-	-	undetermined modification
modification	Ala-1	-	2-naphthalenyl<2-Naph>
modification	Phe-2	-	chloro<Cl>
modification	Ala-3	-	3-pyridinyl<3Py>
modification	Lys-8	-	1-methylethyl<i-Pr>

M. Borin

08/21/97

SEQ 1 AFASYELKPA

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HITS AT: 1-10

AN 126:152828 CA

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CODEN: PIXXD2

PI WO 9640757 A2 961219

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AI WO 96-US9852 960607

PRAI US 95-480494 950607

DT Patent

LA English

REFERENCE 1

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PA Indiana University Foundation, USA; Roeske, Roger W.

SO PCT Int. Appl., 52 pp.

CODEN: PIXXD2

PI WO 9640757 A2 961219

DS W: AU, CA, JP, US

RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

AI WO 96-US9852 960607

PRAI US 95-480494 950607

DT Patent

LA English

L3 ANSWER 4 OF 11 REGISTRY COPYRIGHT 1997 ACS

RN 186836-23-7 REGISTRY

FS 3D CONCORD; PROTEIN SEQUENCE; STEREOSEARCH

SQL 10

NTE modified

type	-----	location	-----	description
terminal mod.	Ala-1	-		N-acetyl
terminal mod.	Ala-10	-		C-terminal amide
modification	Ala-1	-		2-naphthalenyl<2-Naph>
modification	Phe-2	-		chloro<Cl>
modification	Ala-3	-		3-pyridinyl<3Py>
modification	Lys-8	-		1-methylethyl<i-Pr>

SEQ 1 AFASYELKPA

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HITS AT: 1-10

L3 ANSWER 5 OF 11 REGISTRY COPYRIGHT 1997 ACS

RN 186835-69-8 REGISTRY

FS PROTEIN SEQUENCE; STEREOSEARCH

SQL 10

NTE modified

type	location		description
terminal mod.	Ala-1	-	N-acetyl
terminal mod.	Ala-10	-	C-terminal amide
modification	-	-	undetermined modification
modification	Ala-1	-	2-naphthalenyl<2-Naph>
modification	Phe-2	-	chloro<Cl>
modification	Ala-3	-	3-pyridinyl<3Py>
modification	Lys-8	-	1-methylethyl<i-Pr>

SEQ 1 AFASYNLKPA

=====

HITS AT: 1-10

AN 126:152828 CA

TI LHRH antagonist synthetic peptide analogs for use as cancer inhibitors, contraceptives, or other pharmaceuticals

IN Roeske, Roger W.

PA Indiana University Foundation, USA; Roeske, Roger W.

SO PCT Int. Appl., 52 pp.

CODEN: PIXXD2

PI WO 9640757 A2 961219

DS W: AU, CA, JP, US

RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

AI WO 96-US9852 960607

PRAI US 95-480494 950607

DT Patent

LA English

REFERENCE 1

AN 126:152828 CA

TI LHRH antagonist synthetic peptide analogs for use as cancer inhibitors, contraceptives, or other pharmaceuticals

IN Roeske, Roger W.

PA Indiana University Foundation, USA; Roeske, Roger W.

SO PCT Int. Appl., 52 pp.

CODEN: PIXXD2

PI WO 9640757 A2 961219

DS W: AU, CA, JP, US

RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

AI WO 96-US9852 960607

PRAI US 95-480494 950607

DT Patent

LA English

L3 ANSWER 6 OF 11 REGISTRY COPYRIGHT 1997 ACS

RN 186835-68-7 REGISTRY

FS 3D CONCORD; PROTEIN SEQUENCE; STEREOSEARCH

SQL 10

NTE modified

type	location		description
terminal mod.	Ala-1	-	N-acetyl
terminal mod.	Ala-10	-	C-terminal amide
modification	Ala-1	-	2-naphthalenyl<2-Naph>
modification	Phe-2	-	chloro<Cl>
modification	Ala-3	-	3-pyridinyl<3Py>
modification	Lys-8	-	1-methylethyl<i-Pr>

SEQ 1 AFASYNLKPA

HITS AT: 1-10

L3 ANSWER 7 OF 11 REGISTRY COPYRIGHT 1997 ACS
RN 186835-67-6 REGISTRY
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL 10
NTE modified

type	location	description
terminal mod.	Ala-1	N-acetyl
terminal mod.	Ala-10	C-terminal amide
modification	-	undetermined modification
modification	Ala-1	2-naphthalenyl<2-Naph>
modification	Phe-2	chloro<Cl>
modification	Ala-3	3-pyridinyl<3Py>
modification	Lys-8	1-methylethyl<i-Pr>

SEQ 1 AFASYQLKPA

HITS AT: 1-10

AN 126:152828 CA
TI LHRH antagonist synthetic peptide analogs for use as cancer inhibitors, contraceptives, or other pharmaceuticals
IN Roeske, Roger W.
PA Indiana University Foundation, USA; Roeske, Roger W.
SO PCT Int. Appl., 52 pp.
CODEN: PIXXD2
PI WO 9640757 A2 961219
DS W: AU, CA, JP, US
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
AI WO 96-US9852 960607
PRAI US 95-480494 950607
DT Patent
LA English

REFERENCE 1

AN 126:152828 CA
TI LHRH antagonist synthetic peptide analogs for use as cancer inhibitors, contraceptives, or other pharmaceuticals
IN Roeske, Roger W.
PA Indiana University Foundation, USA; Roeske, Roger W.
SO PCT Int. Appl., 52 pp.
CODEN: PIXXD2
PI WO 9640757 A2 961219
DS W: AU, CA, JP, US
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
AI WO 96-US9852 960607
PRAI US 95-480494 950607
DT Patent
LA English

L3 ANSWER 8 OF 11 REGISTRY COPYRIGHT 1997 ACS
RN 186835-66-5 REGISTRY
FS 3D CONCORD; PROTEIN SEQUENCE; STEREOSEARCH
SQL 10
NTE modified

type	location		description
terminal mod.	Ala-1	-	N-acetyl
terminal mod.	Ala-10	-	C-terminal amide
modification	Ala-1	-	2-naphthalenyl<2-Naph>
modification	Phe-2	-	chloro<Cl>
modification	Ala-3	-	3-pyridinyl<3Py>
modification	Lys-8	-	1-methylethyl<i-Pr>

SEQ 1 AFASYQLKPA

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HITS AT: 1-10

L3 ANSWER 9 OF 11 REGISTRY COPYRIGHT 1997 ACS

RN 183552-38-7 REGISTRY

FS PROTEIN SEQUENCE; STEREOSEARCH

SQL 10

NTE modified

type	location		description
terminal mod.	Ala-1	-	N-acetyl
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modification	Ala-1	-	2-naphthalenyl<2-Naph>
modification	Phe-2	-	chloro<Cl>
modification	Ala-3	-	3-pyridinyl<3Py>
modification	Tyr-5	-	methyl<Me>
modification	Lys-8	-	1-methylethyl<i-Pr>

SEQ 1 AFASYNLKPA

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HITS AT: 1-10

REFERENCE 1

AN 127:104336 CA

TI Methods for treating prostate cancer with LHRH antagonists

IN Garnick, Marc B.; Molineaux, Christopher J.; Gefter, Malcolm L.

PA Pharmaceutical Peptides Incorporated, USA

SO PCT Int. Appl., 40 pp.

CODEN: PIXXD2

PI WO 9722357 A1 970626

DS W: AU, CA, JP

RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

AI WO 96-US18911 961125

PRAI US 95-573109 951215

DT Patent

LA English

L3 ANSWER 10 OF 11 REGISTRY COPYRIGHT 1997 ACS

RN 105217-96-7 REGISTRY

FS PROTEIN SEQUENCE

SQL 10

NTE modified

type	location		description
stereo	Phe-2	-	D
stereo	Ala-3	-	D
stereo	Glu-6	-	D

AFASYNLKPA
SEQ 1 PFASYELRPG

HITS AT: 1-10

REFERENCE 1

AN 105:209404 CA
TI Peptides containing an aliphatic-aromatic ketone side chain
IN Rivier, Jean Edouard Frederic; Anderson, Harry Alec; Wylie, Walker
Vale, Jr.
PA Salk Institute for Biological Studies, USA
SO Eur. Pat. Appl., 34 pp.
CODEN: EPXXDW
PI EP 192492 A2 860827
DS R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE
AI EP 86-301278 860221
PRAI US 85-704299 850222
DT Patent
LA English

L3 ANSWER 11 OF 11 REGISTRY COPYRIGHT 1997 ACS
RN 103733-05-7 REGISTRY
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL 10
NTE modified

type	location	description
stereo	Phe-2 - D	
stereo	Ala-3 - D	
stereo	Glu-6 - D	
stereo	Ala-10 - D	

SEQ 1 PFASYELRPA

HITS AT: 1-10

REFERENCE 1

AN 105:191605 CA
TI New effective gonadotropin releasing hormone antagonists with
minimal potency for histamine release in vitro
AU Rivier, Jean E.; Porter, John; Rivier, Catherine L.; Perrin,
Marilyn; Corrigan, Anne; Hook, William A.; Siraganian, Reuben P.;
Vale, Wylie W.
CS Clayton Found. Lab. Peptide Biol., Salk Inst., La Jolla, CA, 92037,
USA
SO J. Med. Chem. (1986), 29(10), 1846-51
CODEN: JMCMAR; ISSN: 0022-2623
DT Journal
LA English

d his

(FILE 'HOME' ENTERED AT 12:32:55 ON 22 AUG 1997)

FILE 'REGISTRY' ENTERED AT 12:33:06 ON 22 AUG 1997

L1 22 S AFASYNLKPA/SQEF
 L2 11 S L1 AND GLN-6/NTE
 L3 11 S L1 NOT L2
 L4 0 S US 95-480494/PRAI

FILE 'CAPLUS' ENTERED AT 12:44:14 ON 22 AUG 1997

FILE 'REGISTRY' ENTERED AT 12:44:29 ON 22 AUG 1997

SET SMARTSELECT ON
 L5 SEL L1 1- CHEM : 25 TERMS
 SET SMARTSELECT OFF

FILE 'CAPLUS' ENTERED AT 12:44:32 ON 22 AUG 1997

L6 5 S L5
 L7 0 S US 95-480494/PRAI
 L8 0 S US 95-480494
 L9 0 S 480494
 L10 0 S 480494/BIB

FILE 'REGISTRY' ENTERED AT 12:48:15 ON 22 AUG 1997

L11 0 S L1 AND ASN-6/NTE

FILE 'CAPLUS' ENTERED AT 12:52:36 ON 22 AUG 1997

=> d bib, abs 16 1-5

L6 ANSWER 1 OF 5 CAPLUS COPYRIGHT 1997 ACS
 AN 1997:501415 CAPLUS
 DN 127:104336
 TI Methods for treating prostate cancer with LHRH antagonists
 IN Garnick, Marc B.; Molineaux, Christopher J.; Gefter, Malcolm L.
 PA Pharmaceutical Peptides Incorporated, USA
 SO PCT Int. Appl., 40 pp.
 CODEN: PIXXD2
 PI WO 9722357 A1 970626
 DS W: AU, CA, JP
 RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT,
 SE
 AI WO 96-US18911 961125
 PRAI US 95-573109 951215
 DT Patent
 LA English
 AB Methods for treating prostate cancer are disclosed. The methods of the invention generally feature administration to a subject of an LHRH antagonist, in combination with a second therapy. In one embodiment, this second therapy is the performance of a procedure that removes or destroys prostatic tumor tissue, such as radical prostatectomy, cryosurgery or radiation therapy (external or interstitial). In another embodiment, the second therapy is

*Caplus
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*Asn or blue or
 The cl
 pas - n 6/
 Spep
 (better read
 the following
 Registry
 report)*

treatment with an LHRH agonist, either simultaneous with or subsequent to LHRH antagonist therapy. The methods of the invention can further involve administering an antiandrogen and/or an inhibitor of sex steroid biosynthesis to the subject in combination with the LHRH antagonist. Methods for inhibiting the LHRH agonist-induced hormone surge, whatever its clin. setting, are also disclosed. These methods generally involve administration of an LHRH antagonist in combination with the LHRH agonist. Complete suppression of the LHRH agonist-induced hormone surge has been achieved by pretreatment with a sustained-release formulation of LHRH antagonist.

L6 ANSWER 2 OF 5 CAPLUS COPYRIGHT 1997 ACS
AN 1997:168540 CAPLUS
DN 126:152828
TI LHRH antagonist synthetic peptide analogs for use as cancer inhibitors, contraceptives, or other pharmaceuticals
IN Roeske, Roger W.
PA Indiana University Foundation, USA; Roeske, Roger W.
SO PCT Int. Appl., 52 pp.
CODEN: PIXXD2
PI WO 9640757 A2 961219
DS W: AU, CA, JP, US
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
AI WO 96-US9852 960607
PRAI US 95-480494 950607
DT Patent
LA English
OS MARPAT 126:152828
AB Many novel LH-releasing hormone(LHRH) antagonist peptide analogs or peptide mimetics, pharmaceutical compns. thereof, and methods of use thereof, are disclosed. The LHRH antagonist comprises a peptide compd., wherein a residue of the peptide compd. corresponding to the amino acid at position 6 of natural mammalian LHRH comprises a hydrophilic N-acyl moiety, a dipolar moiety, a sulfonium moiety, a receptor-modifying moiety or a small polar moiety. LHRH antagonist peptides are useful as inhibitors of sex hormone-dependent cancers (e.g., prostate cancer). LHRH antagonist peptides are also useful as contraceptive agents. The peptides can be used to treat other LHRH-related disorders as well, such as precocious puberty or premenstrual syndrome. The anti-ovulatory and histamine release activity of LHRH antagonists are compared. S.c. injections of LHRH antagonists suppressed plasma testosterone levels.

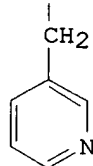
L6 ANSWER 3 OF 5 CAPLUS COPYRIGHT 1997 ACS
AN 1996:696047 CAPLUS
DN 126:26943
TI Structure-activity studies of GnRH antagonists having dipolar residues
AU Guo, L.; Tian, Z.; Edwards, P. J.; Zhang, Y. L.; Shobana, N.; Roeske, R. W.
CS School Medicine, Indiana University, Indianapolis, IN, 46202, USA
SO Pept.: Chem., Struct. Biol., Proc. Am. Pept. Symp., 14th (1996), Meeting Date 1995, 665-666. Editor(s): Kaumaya, Pravin T. P.; Hodges, Robert S. Publisher: Mayflower Scientific, Kingswinford, UK.
CODEN: 63NTAF
DT Conference
LA English
AB The authors report the synthesis of several GnRH antagonists having a D-Lys(ONic), D-Pal(N-O), or D-Pal(CH₂COOH) residue in position 6 or 3 along with their antioviulatory (AO) effects and histamine releasing toxicity (HRT). Compared with the antagonist D-Glu(taurine)6, GnRH-D-Pal(N-O)6 has almost the same level of HRT

'but much better AO activity, 50% inhibition of ovulation at a dose of 1 .mu.g in rats. GnRH D-Lys(ONic)6 and D-Pal(CH2COOH)6 also have low HRT and good AOA of 1/8 and 6/8 at 1.0 .mu.g. Substitution of N-Me-Tyr5 for Tyr5 does not influence AOA and HRT to any extent. Replacement of D-Pal(N-O)6 by D-Pal(N-O)3 increases HRT remarkable from 145 to 25 .mu.g/mL.

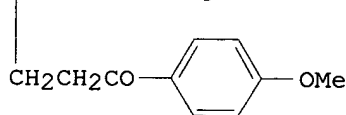
L6 ANSWER 4 OF 5 CAPLUS COPYRIGHT 1997 ACS
 AN 1986:609404 CAPLUS
 DN 105:209404
 TI Peptides containing an aliphatic-aromatic ketone side chain
 IN Rivier, Jean Edouard Frederic; Anderson, Harry Alec; Wylie, Walker Vale, Jr.
 PA Salk Institute for Biological Studies, USA
 SO Eur. Pat. Appl., 34 pp.
 CODEN: EPXXDW
 PI EP 192492 A2 860827
 DS R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE
 AI EP 86-301278 860221
 PRAI US 85-704299 850222
 DT Patent
 LA English
 GI

R1-X1-X2-X3-X4-X5-X6(R2)-X7-Arg-Pro-R3 I

Ac-?-D-2NAL-D-Phe(4Cl)-D-NH-CH-CO-Ser-Arg-



D-NH-CH-CO-Leu-Arg-Pro-D-Ala-NH2



II

AB Peptides I [R1 = H, acyl; X1 = dehydro-Pro, Pro, D-Phe, .beta.-D-NAL, etc.; X2 = His, D-Phe(Cl), D-Phe(Br), D-Phe(NO2), etc.; X3 = .beta.-D-NAL, Trp, D-3-(pyridyl)alanyl, etc.; X4 = Ser, Orn, etc.; X5 = Tyr, Arg, Phe(3Me), etc.; X6 = Gly; R2 = (CH2)n COR4; n = 1-3; R4 = aryl; X7 = Leu, Nle, etc.; R3 = Gly-NH2, D-Ala-NH2, (un)substituted amino, ureido] (.beta.-D-NAL = .beta.-2-naphthyl-D-alanyl) were prepd., and they are useful as ovulation inhibitors (no data). Decapeptide II (contg. a benzoylethyl group) was prepd. by solid-phase peptide synthesis.

L6 ANSWER 5 OF 5 CAPLUS COPYRIGHT 1997 ACS
 AN 1986:591605 CAPLUS
 DN 105:191605
 TI New effective gonadotropin releasing hormone antagonists with minimal potency for histamine release in vitro
 AU Rivier, Jean E.; Porter, John; Rivier, Catherine L.; Perrin, Marilyn; Corrigan, Anne; Hook, William A.; Siraganian, Reuben P.; Vale, Wylie W.
 CS Clayton Found. Lab. Peptide Biol., Salk Inst., La Jolla, CA, 92037,

M. Borin 08/21/97

USA
SO J. Med. Chem. (1986), 29(10), 1846-51
CODEN: JMCMAR; ISSN: 0022-2623
DT Journal
LA English
OS CASREACT 105:191605; CJACS
AB In order to minimize the adverse effect of histamine release of some gonadotropin releasing hormone (GnRH) antagonists, e.g. [Ac-D-2-Nal1, D-4-F-Phe2, D-Trp3, D-Arg6]-GnRH [I, D-2-Nal = 3-(2-naphthyl)-D-alanine residue], new structures with modifications at positions 1, 2, 3, 5, 6, 7, and 10 were synthesized by the solid-phase method on the methylbenzylhydramine resin and they were tested in rats by in vivo and in vitro assays. [Ac-D-2-Nal1, D-4-Cl-Phe2, D-3-Pal3, Arg5, D-4-(p-methoxybenzoyl)-2-aminobutyric acid6, D-Ala10]-GnRH [D-3-Pal = 3-(3-pyridyl)-D-alanine residue] was one of the most potent analogs of this series, causing a 100% inhibition of ovulation at 5 .mu.g/kg or less. Release of histamine was obsd. at doses 10-25 times that required for I. Thus, introduction of arginine in position 5 with a hydrophobic amino acid in position 6 is compatible with high potency in several biol. systems and results in compds. with lowered potency to release histamine compared to homologous peptides with tyrosine in position 5 and D-arginine in position 6.

=> d his

(FILE 'HOME' ENTERED AT 12:32:55 ON 22 AUG 1997)

FILE 'REGISTRY' ENTERED AT 12:33:06 ON 22 AUG 1997

L1 22 S AFASYNLKPA/SQEF
L2 11 S L1 AND GLN-6/NTE
L3 11 S L1 NOT L2
L4 0 S US 95-480494/PRAI

FILE 'CAPLUS' ENTERED AT 12:44:14 ON 22 AUG 1997

FILE 'REGISTRY' ENTERED AT 12:44:29 ON 22 AUG 1997

SET SMARTSELECT ON
L5 SEL L1 1- CHEM : 25 TERMS
SET SMARTSELECT OFF

FILE 'CAPLUS' ENTERED AT 12:44:32 ON 22 AUG 1997

L6 5 S L5
L7 0 S US 95-480494/PRAI
L8 0 S US 95-480494
L9 0 S 480494
L10 0 S 480494/BIB

FILE 'REGISTRY' ENTERED AT 12:48:15 ON 22 AUG 1997

L11 0 S L1 AND ASN-6/NTE

FILE 'CAPLUS' ENTERED AT 12:52:36 ON 22 AUG 1997

=> s 11-16 s480494/1

SAVED L# LIST NAME MAY NOT BE USED IN QUERIES 'S480494/L'
Saved L# lists must be activated before they are used in search profiles. Enter "ACTIVATE" followed by the saved name (including /L) at an arrow prompt (=>). Use the L#s assigned to the answer set in your search profile.

=> s 11-16 c480494/1

SAVED L# LIST NAME MAY NOT BE USED IN QUERIES 'C480494/L'
Saved L# lists must be activated before they are used in search
profiles. Enter "ACTIVATE" followed by the saved name (including /L)
at an arrow prompt (=>). Use the L#s assigned to the answer set in
your search profile.

=> save 11-16 s480494/1

'S480494/L' IN USE

A single name cannot be used for two saved items at the same time.
Enter "Y" if you wish to replace the current saved name with a new
definition. Enter "N" if the current saved definition must be
preserved. You may then reenter the SAVE command with a different
saved name. Enter "DISPLAY SAVED" at an arrow prompt (=>) to see a
list of your currently defined saved names.
REPLACE OLD DEFINITION? Y/(N):n

=> save 11-16 c480494/1

L# LIST 'L1-L6' HAS BEEN SAVED AS 'C480494/L'

=> log h

COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	13.24	209.70
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	-2.42	-2.90

SESSION WILL BE HELD FOR 60 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 13:00:33 ON 22 AUG 1997